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Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

NORTHERN IRELAND, GOVERNMENT OF: **Report on Health and Local Government Administration in Northern Ireland during the Year ended 31st December, 1958.** Cmnd. 406. pp. ix + 113, 5 graphs. 1959. Belfast: H.M. Stationery Office. [6s.]

This is a comprehensive report on similar lines to that of the previous year [this *Bulletin*, 1959, v. 34, 405].

Dr. F. F. MAIN, the Chief Medical Officer, writes a valuable introduction. The population, estimated at 1,402,300, is slowly increasing. There is little change from 1958 in the birth, marriage and death rates which for 1958 were 21·6, 6·6 and 10·8 per 1,000 population. The rates of infant and maternal mortality at 28 and 0·5 per 1,000 live births were the lowest yet recorded. The death rate from tuberculosis, 11 per 100,000 population, was also a record low and led to the winding up of the Northern Ireland Tuberculosis Authority as a separate administrative body as it appeared to be no longer necessary. Cancer is a major problem with a death rate of 160·7 per 100,000 population and steps have been taken to start a registration scheme on the lines of that operating in Great Britain and to develop radiotherapeutic services.

The incidence of poliomyelitis was low and an unexpected finding was that in over half the patients where typing of the virus was undertaken it was Type III: in 1957 only Type I had been isolated. Deaths from whooping-cough increased from 2 in 1957 to 8 and vaccination against this disease at an early age is advocated. Gastro-enteritis in children under 2 years caused 29 deaths. There was no death from diphtheria, measles or scarlet fever.

The total estimated expenditure on the hospital and related services for 1958–9 was £12,772,000 of which £2,541,000 was for capital. There are 16,019 beds including 6,349 in mental hospitals and 804 in "special care" institutions. There are 325 consultants and specialists: there is difficulty in filling junior hospital posts.

The recovery rate of those discharged from mental hospitals was 31·45% and when those "relieved" are added the percentage is 77·67. The first section of a new colony for "special care" patients has been opened and contains 500 beds. The number of beds for the treatment of tuberculosis was reduced during the year from 1,400 to 1,263 and the attendances at chest clinics from 71,373 in 1957 to 68,613. There were 25,671 vaccinations with BCG in 1957 and 22,622 in 1958.

The calls on the ambulance, laboratory and blood transfusion services are all increasing.

The General Health Services are administered by a separate Board. At the end of the year there were 740 doctors on the Board's medical list: 6 fewer than at the beginning. Northern Ireland has more general practitioners per 1,000 population than any other part of the United Kingdom: 48% of the doctors practise in partnership. This compares with 20% in 1948 and 67% in England and Wales in 1957. The cost of the Dental Scheme and that of drugs are slowly rising.

The percentage of domiciliary confinements is falling and is now 36·5 compared with 52·4 in 1955. Attendances at local authority ante-natal clinics are low but at child welfare clinics they remain high. The 203 full- and 9 part-time health visitors paid 188,932 visits to nursing mothers and 274,666 to children between 1 and 5.

Of the 272,282 children examined in school 0·5% were in poor, and 19·5% in only fair, health.

The welfare services provided accommodation for 1,500 persons of whom all save 80 were aged, infirm or handicapped. Some nursing care is provided in welfare homes.

The statutory survey showed that out of 376,324 houses in the country 4% were unfit for human habitation and ought to be closed or demolished but only 416 houses had been so dealt with though a number

of re-development schemes are being prepared. The provision of public water supplies and sewerage proceeds apace: since 1945 £22m. has been expended. [Except for housing, which was impeded by lack of finance, this report shows a satisfactory year's work.]

Allen Daley

ROYAL SOC. PROMOTION HEALTH J. 1959, July–Aug., & Sept.–Oct., v. 79, Nos. 4 & 5. **Health Congress at Harrogate, April 27–May 1, 1959.**

Lord COHEN opened the conference by surveying the advances made in recent times in the prevention and cure of disease, and commenting on the many problems still unsolved, and on the need for research.

Thereafter the conference took its accustomed course. Jonas E. SALK (pp. 310–322) spoke on vaccination against poliomyelitis and Philip DRINKER (pp. 323–329) on air pollution; each of these papers was a summary of existing information by a master of his subject. The Radiation Section concerned itself with radiation levels and the design of nuclear power stations, and the Mental Health Section with the changing pattern of the mental health services and the epidemiology of mental illness, both subjects of increasing importance.

The conference has always thrown a wide net, and on this occasion the architects were in it to discuss the development of towns (here called urban centres), and the effect of motor vehicles on planning, and the public health inspectors looked at environmental health practice in the United States, with a sense of the change in emphasis towards accident prevention, radiation and atmospheric problems, and hospital sanitation—by which is meant the prevention of hospital infection.

In the section on World Health and Tropical Hygiene the importance of economics and the social sciences received attention—as they should—and in particular by Professor T. H. DAVEY (pp. 407–412) in relation to the tropics, who stresses the fact that Africans should not be expected to adopt European patterns of life without modification to their own conditions.

The Occupational Health section discussed rehabilitation, and the contributions made by the hospital services, the local authorities and the statutory and voluntary services.

The veterinarians see the approaching end of bovine tuberculosis.

In an assessment of the incidence of notifiable diseases W. H. BRADLEY (pp. 475–485) comments on the change which has taken place in the common infections of Britain since the days when plague, typhus, smallpox and cholera dominated the scene; but the future may not be as propitious as at one time it seemed, if the population problem is not solved. S. L. WRIGHT (pp. 485–490) discusses control of infections, with emphasis on the continuing importance of sanitary measures. G. I. WATSON (pp. 494–498) comments on problems of notification.

Problems relating to insecticides were discussed by J. R. BUSVINE (pp. 505–510) who spoke on resistance, and T. F. WEST (pp. 511–517) on techniques of use.

The Chadwick Lecture was given by Gordon M. FAIR (pp. 524–545), who ranged over fluoridation of water, air pollution and radiation—ending with the warning that microchemical forces in the environment are becoming more complex, and are of our own making.

The Hospitals Section concerned itself with planning and with a conception of a hospital centre; this is envisaged as a much more comprehensive unit than it now usual.

Children in hospital was the theme of the conference of Health Visitors, and the Family Section discussed such matters as marriage, working mothers, and family guidance. Domiciliary care was also the subject of several papers, with emphasis on the older patients. The Food and Nutrition Section dealt with food hygiene and the protection of the consumer, the Veterinary Section with slaughterhouses, the Public Health Inspectors' Conference debated their own important functions and the standards to be applied in matters of housing with much technical information, and the engineers and surveyors argued about heating and about sanitary fittings.

It is not possible to give a coherent account of a great conference in a limited space of print. The mere recital of the main subjects discussed is enough to indicate how wide is the present conception of public health duties and interests. One impression to be gained from such a conference as this is that we now pay more attention than we once did to the mental problems of the community, and that we are concerned with happiness as well as physical well-being.

Charles Wilcocks

NORMAN, L. G. **The Health of London's Travelling Public.** *Roy. Soc. Promotion Health J.* 1959, May–June, v. 79, No. 3, 229–40, 2 figs. [15 refs.] Discussion 240–41.

This paper contains an analysis of the composition and habits of the London travelling public, most of whom are adults and travel to work by some form of transport. The author discusses the effect of the existing travel arrangements on health, and comment is made on the facilities for spread of the respiratory infections, with an interesting graph which shows the consistently higher absence rate for sickness in bus conductors than in bus drivers. Nevertheless, epidemiological and bacteriological evidence does not suggest that any serious spread of infection takes place in Underground trains.

The author summarizes the investigations carried out on internal combustion engines and the gases they emit, and concludes that "there is no evidence to show that the health of London's travelling public is in any way affected by the use of diesel-engined road vehicles". Smoking in public vehicles is discussed, but largely because of its nuisance effect rather than any effect on health.

On the subject of comfort in riding the author makes a sound point when he says that "worry is harmful and work is beneficial; the anxiety and stress of travelling home in the rush hour are therefore more harmful than working for an extra 15 minutes or so and travelling home in comfort."

Charles Wilcocks

WHITE, T. H. **Some Medical Aspects of Social Progress in an African Industrial Community.** *East African Med. J.* 1959, Nov., v. 36, No. 11, 585–94, 5 graphs. Discussion 594–5 [THOMAS, A. T. G.].

In an earlier paper [this *Bulletin*, 1955, v. 30, 872] the author gave an account of his experiences as medical officer of the Magadi Soda Company in Kenya, in medical charge of a multi-racial community of nearly 3,000 people. One of the important factors is the stability of the population, and this has improved recently, largely because the housing situation has been greatly improved with the construction of flats for African families in the restricted space available. Water supply and sanitation have also been improved. The result is that whereas in 1950–52 the number of pre-employment medical examinations was about 120% of the labour force per annum, the figure for 1957 was about 35% indicating a far smaller turnover of employees. During the period of unrest a few years ago there was considerable travel to and from the reserves, largely by women, but not by children, and more women had their babies at Magadi than before, probably because it was a safe place, and housing was good. Measles and whooping-cough show fluctuations in incidence over the past few years, and tuberculosis seems to be increasing; these changes are related to the population fluctuations.

The author pays much attention to the social conditions of his patients, and this approach is strongly supported by A. T. G. THOMAS in his discussion of the paper; it is important "to get a man settled into a decent house with his family". He comments on duodenal ulcer as a stress disease—"Personal and social environment is often the biggest factor in causing the disease and it can be prevented and cured by a study of the individual's emotional personal problems and their adjustment." This is an illustration of a wider principle. *Charles Wilcocks*

SOUTHALL, Aiden, W. & GUTKIND, Peter C. W. **Townsmen in the Making. Kampala and its Suburbs.** With a foreword by A. Kalule SEMPA. 2nd Edition. pp. xiii + 248, 3 loose-leaf folding maps (1 coloured). 1957. Kampala: East African Institute of Social Research, P.O.Box 262, Uganda. London: Kegan Paul Trench Trubner & Co. Ltd., 43, Great Russell Street, W.C.1. [8s.]

This is a report of an extensive survey of an area of dense African population in Uganda, and an area of intermediate position between town and country; the method of investigation involved interviews with members of all households at first and later random samples taken over a larger area.

The first part refers to the town of Kampala and the Kibuga [capital], the second to Kisenyi, the third to Mulago and the fourth to administrative problems in Greater Kampala. The various sections deal with such subjects as history, land and housing, economic activity, marriage and local government, but the small section which would most interest readers of this *Bulletin* is that dealing with attitudes to sickness in Mulago (pp. 110–12), in the neighbourhood of the great hospital.

Questions of disease play a great part in the conversation of the people, and their attitude is ambivalent. They distinguish between Kiganda disease and European disease, and they tend to seek help first from the traditional African "doctors" who believe that diseases have causes quite different from those acceptable to western medicine, but who are ready to give precise diagnoses and prescribe clear treatments. They give the patients much mental satisfaction, and if they fail the patient is quite ready to seek European medicine. Africans remark that European doctors only give injections, and Kiganda diseases do not respond to that treatment; moreover, any failure of European treatment tends to send them to the traditional treatment. One is reported to have said that questions are not answered by the African doctors at the Mulago hospital but that traditional "doctors" will always tell what is the matter with the patient.

[The problem of communication is as important in medicine as in other spheres.] *Charles Wilcocks*

SACHS, S. B. **The Meadowlands Method: an Experiment in an Integrated Curative Service.** *South African Med. J.* 1959, Sept. 19, v. 33, No. 38, 781–4.

In Africa today, every administration is faced with the ever increasing demand on beds by a population which is beginning to appreciate the value of European medicine. So heavy has the pressure become that the Transvaal Administration has launched an interesting experiment in Meadowlands in Johannesburg where in 1957 it started a clinic under the control of the central Baragwanath Hospital.

Meadowlands with its 50,000 Africans is a modern location with good sanitation. A special innovation was the construction of a clinic on the principle of "patient flow". No large central waiting hall was built, but a waiting place provided next to each consulting room. Patients attended the clinic for every type of ailment and there has been very good liaison between the central, provincial and council authorities. To reach the home of the patient a district nursing service was introduced and this meant that patients could be discharged earlier from the main hospital where beds were badly needed and yet be under observation. The clinic will gradually take over more deliveries from the main hospital. 6 to 7 beds will be provided there for night deliveries as well as X-ray and laboratory facilities, and follow-up treatment is to be given to patients in their own environment. Difficult cases are seen by specialists sent out by the main hospital.

One of the great drawbacks of outpatient work in Africa is the very large number of people seeking aid, often for very little reason. Because of this the examination itself is often only cursory and many a medical officer soon becomes disheartened. But in the Meadowlands clinic the emphasis is more positive and therefore on promotive and preventive medicine. It aims

at *health recovery*. In order to achieve this two main concepts are applied:—(1) That the entire person as well as the circumstances of his family and community be considered. (2) That the pathological processes be extended to include relationship to the environment and psychosomatic host reaction.

Four main principles are practised:—

(1) *Prevention of Disease at the Level of Early Diagnosis.* An example is the use of the miniature X-ray by means of which pulmonary tuberculosis can be readily detected. The whole population of Meadowlands is being X-rayed. Another example is ante-natal examination.

(2) *Selection.* "Special Cases" are dealt with separately and they are observed for long periods. This group would include those complaining of cough, obscure fever, loss of weight and cardiovascular disease.

(3) *Observation over a Period of Time.* Instead of merely being observed while he is in hospital, the patient is followed up by visits to his home after his discharge.

(4) *Health Recovery* by which possible factors are corrected. The scheme is well organized. The Meadowlands area is divided into two units, each under two medical officers who are responsible for the clinic, the maternity services, the district nursing service and the "special cases." *M. Gelfand*

VITAL STATISTICS

MELNOTTE, P., NEIMANN, N., MANCIAUX, M. & DALER, S. Pathologie pédiatrique régionale de la France du Nord-Est au cours des vingt dernières années. [**Regional Morbidity and Mortality of Children in North-East France during the Last 20 Years**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1959, Oct.–Nov., v. 7, No. 7, 571–96, 2 maps & 13 graphs. [Refs. in footnotes.]

The region studied in this report was Lorraine and included the départments of Ardennes, Aube, Marne, Haute-Marne, Meurthe-et-Moselle, Meuse, Moselle, Vosges which comprise 9% of the territory of France. The population of the region was slightly over 3 millions and was younger than that of France as a whole, 42% of the population were aged under 25 years compared with 38% for France. The birth rate since 1946 has been considerably larger than the rate for France, in 1956 the rate was 22 per 1,000 for Lorraine and 18 for France. The infant mortality, which has steadily fallen since 1945, follows the same pattern as in France but at a slightly higher level, the rate per 1,000 live births in 1957 was 30·6 in Lorraine and 29·0 in France. The mining districts of the region experienced a higher infant mortality than the remainder. 44% of the infant mortality in 1957 was attributed to prematurity and debility, 15% to diseases of the respiratory system and 11% to diseases of the digestive system. The relative importance of accidents as a cause of death among children has increased during the past 15 years from 8·4 to 17·0% for children aged 1–4 and from 15·5 to 34·8% for children aged 5–15 years.

Part 2 of the paper deals with morbidity and mortality in hospitals. Part 3 briefly reviews (a) diseases for which vaccination is available, smallpox, tuberculosis, diphtheria and tetanus and (b) imported diseases, mainly from north Africa.

[The comparisons in this paper are based mainly on proportional mortality and no rates are given so that it is not possible to make comparisons with the actual trends. Thus, although accidents have doubled their relative importance as a cause of death in the pre-school and school child during the past 15 years there is no means of deciding whether the actual death rate has increased or not since the total death rate is not given.] *W. J. Martin*

GROUNDS, J. G. **The Population Structure and some Vital Statistics of a Rural Area in Kenya.** *East African Med. J.* 1959, Dec., v. 36, No. 12, 644–8, 1 map.

During 1957–58 a register was compiled for persons in 7 carefully defined rural areas in South Nyanza, Kenya, and on a fixed day everybody was seen and their age and sex entered; altogether there were 2,425 males and 2,643 females. The ages of the females tended to be overestimated. One year after the survey the areas were re-visited and the births and deaths that had occurred during the year were recorded. The findings are shown in tables. From this information it was estimated that the birth rate was 46·4 per 1,000 population, infant mortality was 147 and neonatal mortality 38 per 1,000 live births, the stillbirth rate was 95 per 1,000 total births and the crude death rate was 21·4 per 1,000 population. The rate of increase in the population was 2½%. *W. J. Martin*

MATERNAL AND CHILD HEALTH

RING, Eileen. **Health Education in the Maternal and Child Welfare Services.** *J. Roy. Inst. Pub. Health & Hyg.* 1960, Jan., v. 23, No. 1, 11–19. [15 refs.]

The first section of this paper recounts the quite remarkable reductions in maternal and infant mortality in recent decades. Maternal mortality was 40 per 10,000 total births in 1911; in 1958 it was 4. Infant mortality was 153 per 1,000 live births in 1900; in 1958 it was 22·9. The development of the maternal and child welfare centres, of which there are now 5,800, from milk depots and schools for mothers is described.

The next deals with present-day problems of which there are many: 60% of all infant deaths occur in the first week of life chiefly from immaturity, birth injury and asphyxia, congenital malformations and haemolytic disease of the newborn. The perinatal mortality is 35·1 per 1,000 births. As a child grows emotional disturbances and accidents assume great importance. A new hazard is the plastic bag in which children are apt to enclose their heads and a newly recognized one for the newly born is exposure to very low atmospheric temperatures. The social environment, seen at its worst in a "problem" family, is of great importance.

Those engaged in health education must know the facts as the background of their teaching: the giving of instruction must be shared between the hospital and family doctors and the local health authority.

The function of a child welfare centre is the practice of preventive medicine: a change of emphasis is desirable from routine weighing of the infant to a regular assessment of the physical and mental development of the child and giving time to the mother to ask all her questions.

The most important task of the M.O.H. is to impress on "his colleagues the need for the fullest application of preventive measures to reduce further maternal and perinatal mortality and to forestall morbidity in mothers and children". Further "the success of a health education programme will depend on the cooperation of parents" and "the most important requirement in a health education programme is good leadership and a well informed medical and nursing staff conscious of present-day needs".

A central supply of demonstration material and visual aids should be available. *Allen Daley*

STEWART, Alice M. **Environmental Hazards of Pregnancy.** Reprinted from *J. Obstet. & Gynaecol. Brit. Empire.* 1959, Oct., v. 66, No. 5, 739–42.

In the first section of this paper there is an account of the findings already published [this *Bulletin*, 1955, v. 30, 933; 1956, v. 31, 356] of 2 surveys carried out for the purpose of study of the effects of work during pregnancy. In the first survey 1,318 primiparae in Northamptonshire—780 housewives, 285 women who worked in paid employment for less than 28 weeks during the pregnancy and 253 who went out to work for longer periods—were studied during 1952. The second survey included all babies born in Northamptonshire in 1952 and sample populations of babies born in 4 other areas. The findings of these surveys are stated. The incidence of toxaemia was virtually the same in the 3 groups of mothers but there were significant differences between the 3 groups in the proportion of stillbirths, neonatal deaths and premature babies. "In each respect the housewives suffered least and the long-term workers most".

The second part of the paper describes the results of re-examination of 1,201 survey records of mothers to study the possible relationship between physique and toxaemia of pregnancy. The women were classified according to their build (height divided by the cube root of weight) in the physique groups of overweight (body-build index 10·8–12·0), average (index 12·1–13·0) and underweight (index 13·1–14·5). In these groups the incidence of toxaemia was 22·6% in the overweight, 11·9% in the average and 8·1% in the underweight groups.

In the third part of this paper there is a restatement of the findings of the authors of the second paper (*Brit. Med. J.*, 1958, v. 1, 1495) with the conclusion: "We are still prepared to stand by our original statement that a 'typical' X-ray examination *in utero* doubles the risk of leukaemia and cancer in childhood". This statement was based on the results of interview of mothers of 1,299 children who had died of malignant diseases before their tenth birthdays. There is a considerable discussion of this subject with some stress on the fact that the normal risk of malignancy in children up to 10 years of age is small and that even "doubling the risk" for *all* children, *i.e.* by X-ray of all before birth, would add only 60 "extra" deaths to the yearly total. *M. E. Delafield*

STEVENSON, A. C.; WARNOCK, H. A.; DUDGEON, M. Y.; MCCLURE, H. I. **Observations on the Results of Pregnancies in Women Resident in Belfast. I. Data relating to all Pregnancies ending in 1957** [STEVENSON & WARNOCK]. *Ann. Human Genetics.* 1959, Dec., v. 23, Pt. 4, 382–94. **II. Abortions, Hydatidiform Moles and Ectopic Pregnancies** [STEVENSON, DUDGEON & MCCLURE]. *Ibid.*, 395–414. [20 refs.] **III. Sex Ratio with particular reference to Nuclear Sexing of Chorionic Villi of Abortions** [STEVENSON]. *Ibid.*, 415–20.

I. These papers are comprehensive studies of all pregnancies terminating in Belfast in 1957. The data comprised 9,526 pregnancies and included 8,039 single live births, 205 single stillbirths, 121 twin live births, 2 twin stillbirths, 10 twin births one alive and one still, 3 live triple births, 1,127 abortions, 11 ectopic pregnancies and 8 hydatidiform moles. The distribution of parental age, order of pregnancy, outcome of previous pregnancies are given. The outcome of the previous pregnancies is tabulated by maternal age and by order of pregnancy. Consanguinity was low in these data being only 0·44%. Consanguinity was only noted once (second cousins) in parents of a stillborn child and not at all among the parents of a malformed child. There were a total of 120 children, live and stillborn, with gross abnormalities, a rate of 1·4% of the total births. For malformations an appendix gives for each child the place of birth, parental age, sex, outcome of past pregnancies of mother, pregnancy order, maternal hydramnios and anomalies. The incidence of anencephaly in Belfast was high, 4·58 per 1,000 total births Hydramnios complicated 1/3 of the pregnancies resulting in a malformed child and in at least 2% of all pregnancies this condition was a complication.

II. Abortions which formed at least 11·8% of all pregnancies during the year were analysed by parental age, pregnancy order, duration of pregnancy, gynaecological disorders. Criminal abortion does not seem to have been an important factor in the high rate and there is no obvious relationship between abortion and chronic and acute diseases. Abortions were low in the first pregnancy, 8%, and rose steadily to the 5th

pregnancy and then remained fairly constant at between 17–18%. The rate was high at ages under 20, 12·3%, fell to 8·6 at ages 20–24 and then rose steadily to 25·0% at ages 40–44. The role of lethal mutation in determining abortions and foetal deaths is discussed.

III. An attempt was made to determine the sex of abortions by nuclear sexing of chorionic villi and the difficulties of doing this are discussed at some length. The authors conclude that among the abortions studied the male to female ratio was 1·08. *W. J. Martin*

WRIGHT, E. W. **A Variation in the Intermediate School Medical Examination.** *Med. Officer.* 1960, Jan. 1, v. 103, No. 1, 5–8.

This paper is from the Bournemouth Health Department. It develops the idea of a questionnaire completed by parents and teachers as an aid to the more fruitful use of the school medical service. The idea was promulgated by BARASI & CARTWRIGHT [this *Bulletin,* 1957, v. 32, 397; 1958, v. 33, 924].

The experiment was tried in 2 mixed junior schools containing 249 10-year-old children. After the questionnaires to parents and teachers had been despatched the school nurse tested the hearing of each child with an audiometer and the vision with Snellen's charts. The school doctor then studied the returned questionnaires and the nurse's findings, inspected rapidly all the children and saw them during physical exercise periods. He then divided them into 3 groups: (a) examination needed, (b) examination not needed, and (c) for discussion with the teachers and the nurse after which some from (c) were added to (a). The medical examinations were by appointment at a fixed time: the intervals between appointments ranged between 3 and 20 minutes; it was commonly 10 minutes. There were eventually 115 children in group (a): of the rest 26 were to be reviewed in 6 months and in 108 an examination was deemed to be unnecessary. The school nurse did not attend the examinations.

Only 3 parents did not return the questionnaire: in 128 of those completed no abnormality was reported. Parents reported psychological abnormalities in 70 children and teachers in 48. Analyses of the forms are given to show the differences when the father or the mother completed the form and whether or not the mother went out to work. A table shows how the findings differ according to the interest shown by the teacher in the experiment.

This system puts more work on the parents and teachers; it takes slightly more of the doctor's time: the work of the clerical staff is increased by about 50%.

The final sentence is "The suggestion is made that such a scheme, after suitable modification, would be both more efficient and more expensive."

Allen Daley

POLLITT, W. A. **An Investigation of Hearing Defects in Children.** *Med. Officer.* 1960, Jan. 29, v. 103, No. 5, 59–61.

"This investigation resulted from the considerable differences in the findings of two surveys of hearing ability of children in different age groups"

In a township created in an agricultural area near Liverpool about 200 children attending the child welfare clinics under the age of 5 years were tested by the method described by EWING and EWING [this *Bulletin,* 1948, v. 23, 6] and of these no child failed "to pass at the second, if not the first occasion of testing". In comparison with this result it was found that in 1,432 school children in the eighth year age group examined by audiometric sweep test [WITHNELL, this *Bulletin,* 1958, v. 33, 304] 251 failed this test. Subsequent examination of these 251 (5 absentees) by the pure tone audiometer test revealed 111 failures. These 111 children with 37 others referred by parents and teachers and 33 referred by medical staff were examined further. The deafness of these children was of Grade I to IIb of the Ministry of Education grading, and the findings of the cause of deafness are set out in a table. The main causes were otorrhoea (24 cases), retracted or scarred drum (18), wax (19) and perforation of ear drum (15). The fact that 52 (28·7%) of the children failed to attend the examination indicates a disquieting lack of interest in parents. Most of the children were in the lower 3 groups of the Registrar General's social classification.

A short test of the effects of hearing loss on education was carried out. The importance of prevention, quick effective treatment and health education of parents is emphasized. *M. E. Delafield*

HEALTH OF STUDENTS, NURSES AND HOSPITAL STAFFS

HORN, D., COURTS, F. A., TAYLOR, R. M. & SOLOMON, E. S. **Cigarette Smoking among High School Students.** *Amer. J. Pub. Health.* 1959, Nov., v. 49, No. 11, 1497–1511.

A questionnaire on smoking habits was given to 21,980 high school students (aged 13–18 years) in and around Portland, Oregon. Of the boys 25% never smoked, 5% regularly smoked between 1 and 6 cigarettes a week, 13% regularly smoked 1–9 cigarettes a day and 7% regularly smoked 10 or more cigarettes a day; the corresponding figures for girls were 47%, 4%, 8% and 2%. Other groups smoked occasionally or experimented, or had given it up. Factors found to be associated with a high incidence of smoking were (1) cigarette smoking by one or both parents, (2) lack of participation in athletics and other extracurricular activities, (3) lack of scholastic success—indicated by

being substantially older than the average age of the class and (4) low academic ambition. A higher proportion of smokers was also found in the Catholic schools compared with the public high schools; this could not be accounted for by any of the other factors listed.

Various types of education about the ill effects of smoking were carried out at selected schools during the course of one year and the questionnaire was repeated. The results obtained with the second questionnaire have not yet been analysed. *Richard Doll*

CHRONIC CARDIO-RESPIRATORY DISEASES

THORAX. 1959, Dec., v. 14, No. 4, 286–99, 12 figs. **Terminology, Definitions, and Classification of Chronic Pulmonary Emphysema and Related Conditions. A Report of the Conclusions of a CIBA Guest Symposium.**

Following a symposium on chronic pulmonary emphysema and related conditions, certain provisional conclusions and proposals were formulated. These were subsequently reconsidered and modified by a drafting committee, and finally approved with minor reservations by all the participants. There are 4 principal ways in which emphysema may be defined: clinical, *i.e.*, upon a simple descriptive basis, morbid anatomical, functional or physiological, and aetiological. The term emphysema was originally applied by Laennec to a morbid anatomical state. When defined in anatomical terms it has not been found possible to correlate emphysema with any single uniform clinical radiological or functional syndrome. The clinical use of the word should be regarded as presumptive, and only be applied to those cases in which, in the observer's opinion, the defined morbid anatomical changes in emphysema can be confidently asserted to be present. Emphysema is defined as a condition of the lung characterized by increase beyond the normal in the size of air spaces distal to the terminal bronchiole either from dilatation or from destruction of their walls.

A classification is proposed upon a descriptive morbid anatomical basis, since too little is known about pathogenesis to justify a formal pathogenetic basis. This classification is laid down and the terms defined.

The grading of the severity of emphysema was difficult. In focal and centrilobular emphysema, in mild cases less than 25%, in moderate cases 25% to 50%, and in severe cases more than 50% of the lung should be abnormal. Beautifully produced photographs explain what is meant in this respect.

At present the diagnoses "chronic bronchitis", "asthma", and "emphysema" are used without any general agreement about the clinical conditions to which they refer. It appears that chronic bronchitis is often used in Great Britain to describe cases that would be called asthma or emphysema in the United States.

The committee suggests that "chronic non-specific lung disease" be used for the whole group. It may be defined as comprising those subjects with one or more of the following: chronic cough with expectoration, and paroxysmal or persistent excessive breathlessness, which are not solely attributable to: localized lung disease, generalized specific infective lung disease, the pneumoconioses, collagen diseases, and generalized pulmonary fibroses, primary cardiovascular-renal disease, diseases of the chest wall, and psychoneurosis.

For purposes of classification it is suggested that patients are classified according to 3 types of respiratory disorder. (1) chronic or recurrent excessive secretion of bronchial mucus. (2) intermittent obstruction to bronchial air flow. (3) persistent obstruction to bronchial air flow. A table is appended showing the correlation of proposed terminology with current usage.

On the subject of generalized obstructive lung disease, a division into lung impairment, lung insufficiency, and lung failure is suggested.

The use of lung function tests in the study of chronic non-specific lung disease is considered. The function can be divided into ventilatory function, alveolar-capillary function, and pulmonary circulatory function. The type of tests which are considered essential, and those which are recommended are laid down in full.

[This paper is an effort to produce some kind of order in the jungle of diseases which are usually referred to under the headings chronic bronchitis, emphysema and asthma. While its conclusions may not eventually be fully accepted it represents a most praiseworthy effort to produce a basis by which various workers can correlate their findings.] *F. H. Young*

BRITISH J. RADIOL. 1959, May, v. 32, No. 377, 286–305, 27 figs. [17 refs.] **Chronic Bronchitis and Emphysema: a Symposium. I. The Epidemiology of Chronic Bronchitis** [STUART-HARRIS, C. H.] 286–9. **II. Clinical Aspects of Chronic Bronchitis** [OSWALD, N. C.] 289–90. **III. Pathological Findings and Radiological Changes in Chronic Bronchitis and Emphysema** [REID, Lynne; SIMON, G.] 291–305, 27 figs.

The report of this symposium gives an account of our present knowledge of chronic bronchitis and emphysema from various points of view. C. H. Stuart-Harris in his paper (pp. 286–289) indicates the scope of the science of epidemiology in chronic bronchitis. This approach to chronic bronchitis is bedevilled by the task of definition. The epidemiological studies made so far have embodied different approaches, and these are detailed.

4 lines of evidence arise from the study of mortality statistics. Great Britain has the unenviable reputation of being the country with the highest incidence of death from chronic bronchitis, but the differences between different countries are in fact so great that the validity

of the statistics must be suspected. In different countries, chronic bronchitis, emphysema, and, in the United States, asthma may be terms to indicate the same disease.

Secondly, deaths from chronic bronchitis increase steadily with age and show a preponderance in males over females. Thirdly, in England and Wales, the deaths from bronchitis show a preponderance for urban compared with rural areas. Finally, bronchitis appears to be a condition with a remarkable correlation between prevalence and social class.

In the study of morbidity Reid's enquiry into postmen [this *Bulletin*, 1958, v. 33, 1107] shows some remarkable geographical differences with a correlation between sickness and a complex referred to as industrialization. The total invalidism from chronic bronchitis in postmen correlates with fog frequency, and not at all with population or domestic crowding. Absence rate due to bronchitis is much greater in areas where postmen are exposed to a heavy atmospheric pollution, but personal habits may outweigh the incidence of other environmental factors. Little light is thrown on the importance of personal constitution and of heredity.

N. C. Oswald (pp. 289–290) indicates how the terms chronic bronchitis, emphysema, and asthma came into common parlance. In assessing chronic bronchitis from the therapeutic point of view regard must be paid to the importance of excessive mucus, bronchospasm, infection and emphysema. He indicates the general line of treatment that ought to follow assessment of these factors.

Lynne Reid (pp. 291–292) considers that chronic bronchitis is primarily concerned with changes in the bronchi, especially hypersecretion of mucus and damage caused by infection. She considers that in its earlier stages chronic bronchitis would seem to be essentially a hypersecretion of mucus. In well-established cases this hypersecretion is reflected by a hypertrophy of the mucous glands and the goblet cells. Frequently between the attacks there is an absence of cellular infiltration. The irreversible damage caused by infection is more serious peripherally in the small bronchi, bronchioles and respiratory tissue. Owing to the collateral ventilation the obstruction of an airway does not necessarily cause distal collapse. The characteristic progress of chronic bronchitis which leads to respiratory disability seems to be through multiple irregular foci of peripheral damage.

G. Simon (pp. 292–294) observes that on examining over 1,000 plain radiographs of a series of patients suffering clinically from chronic bronchitis, in nearly half there was no evidence of any departure from the normal, and no evidence of any generalized parallel-walled linear shadows.

Small ill-defined homogeneous shadows, roughly circular, seen in many patients probably represent non-tuberculous fibrotic scars.

The X-ray changes observed in cases of pure chronic bronchitis appear to be very slight. Bronchographically a common finding is that of small spiky projections from the undersurface of the main or segmental bronchi. Sometimes there is an excessive change in the calibre of a bronchus here and there between deep inspiration and expiration, but this may be due t changes in the lung tissue rather than the bronchi.

Occlusions of the bronchi after about 5 to 8 genera tions along an axial pathway, or of bronchioles stil more distal are frequent. These appearances suggest functional obstruction to the more distal flow of th medium, either from excessive secretion in the lume or air trapping, and the absence of the normal inspira tory suck, resulting from occlusion of the pathway at more distal level.

Other less usual bronchial abnormalities are detailed

Pathologically, Lynne Reid (pp. 294–303) describe the characteristics of emphysema as an abnorma amount of air in the respiratory part of the lung; mor precisely as a lung condition in which there is a increase beyond the normal in the size of the air space distal to the terminal bronchiole, either from dilatatio or destruction of the walls. She divides it into groups: (1) Dilatation emphysema, in which th respiratory unit is distended but anatomically intact and group (2) Destruction emphysema, in which ther is some degree of destruction, which may even be com plete so that no residue of a respiratory unit can b recognized.

She deals with the dilatation type under headings o spasmodic asthma, compensatory emphysema, obstruc tive emphysema, simple coal-miner's pneumoconiosis and senile emphysema.

In the destructive type of emphysema there is a increase of the size of the unit together with loss o the capillary bed, interruption of the blood supply t the distal part of the acinus, and transformation of th wall of the bronchiole into the structure of a flap-valve

Radiographically, the most characteristic feature o emphysema is an alteration in the balance of hila and peripheral vessels; the main pulmonary arteries ar large, with abrupt reduction of the size of thei branches right from their source.

Simon (pp. 303–305) deals with radiological change in emphysema, and remarks on the following features air excess distributed unevenly giving a relative hyper translucency to the affected area: a low position o the diaphragm with an increase in the anterior posterio diameter of the chest with a widened retrosterna translucency in the lateral view: the diaphragm tend to be flattened, and moves poorly on respiration: th appearance of hypertranslucent avascular zones wit hair-line shadows; these shadows may produce a com plete ring, but more often appear as a curvilinea shadow. Vessels are often crowded together, an nearby vessels appear narrowed and widely space owing to the adjacent bullous areas. The main hila vessels, peculiarly the arterial trunks, seem larger tha normal. The major pulmonary intrapulmonary vessel tend to appear small and inconspicuous.

Radiological appearances are frequently unchange over a number of years although the patient ma deteriorate. The X-ray diagnosis of emphysema reasonably accurate where all the changes are presen namely those relating to the diaphragm and thorac cage, those indicating bullae and those of the cardio vascular system. Correlation between the X-ray appea ances with the clinical conditions is frequently, bu by no means always, close. *F. H. Young*

LEES, A. W. & MCNAUGHT, W. **Bacteriology of Lower-Respiratory-Tract Secretions, Sputum, and Upper-Respiratory-Tract Secretions in "Normals" and Chronic Bronchitics.** *Lancet.* 1959, Dec. 19, 1112–15, 1 fig. [13 refs.]

Bronchial secretions uncontaminated by secretions from the upper respiratory tract were obtained for bacteriological examination from 14 patients with small healing tuberculous lung lesions and from 28 with chronic bronchitis by means of special swabs. The tuberculous patients were symptomless and were considered to have normal bronchial tracts. The bronchial swab was a cotton-wool swab on the end of a 60 cm. wire contained in a long glass tube. The glass tube was passed down inside a bronchoscope with the swab retracted and the sample obtained under direct vision by pushing the swab out against the mucosa and returning it into its glass tube before the tube was withdrawn from the bronchoscope. Bacteriological examination of a nasal swab, a throat swab, sputum, and saliva, from each of the patients was also done.

All 14 bronchial swabs from the patients with normal bronchi were sterile. *Haemophilus influenzae*, pneumococci, or both these organisms were cultured from bronchial swabs of 21 of 28 patients with bronchitis. Coliforms were found in 3 swabs and coagulase-positive staphylococci and haemolytic streptococci in one swab each from the bronchitic patients. *H. influenzae* and pneumococci were frequently found in the sputum and in the mouths and throats of the normal patients whose bronchial swabs were sterile.

The authors consider that their work further strengthens the association of *H. influenzae* and pneumococci with chronic bronchitis, and suggest that the bacteriological examination of sputum is of little practical value in the clinical management of bronchitis [this *Bulletin*, 1958, v. 33, 555]. *I. B. R. Duncan*

LEES, A. W. & MCNAUGHT, W. **Non-Tuberculous Bacterial Flora of Sputum and of the Upper and Lower Respiratory Tract in Pulmonary Tuberculosis.** *Lancet.* 1959, Dec. 19, 1115–17. [13 refs.]

The authors examined bacteriologically the same types of respiratory specimens as in their earlier investigation [see above] from 4 other groups of patients. These were: (A) 16 patients with minimal tuberculosis without bronchitis; (B) 16 patients with extensive tuberculosis without bronchitis; (C) 16 patients with extensive tuberculosis complicated by chronic bronchitis; and (D) 9 patients with histologically proven bronchial carcinoma.

Bronchial swabs from all 16 patients in group A, and from all but 2 in group B were sterile. Pathogens, particularly *Haemophilus influenzae* and pneumococci, were isolated from bronchial swabs of 12 of 16 patients in group C, and in 6 of 9 in group D.

It is pointed out that *H. influenzae* and pneumococci appear to cause bronchitis complicating pulmonary tuberculosis, and that sputum production and dyspnoea in such patients may wrongly be attributed to the tuberculous process itself, rather than to the bronchitis. The bronchitis should be treated with antibiotics in the same way as bronchitis unassociated with tuberculosis.

I. B. R. Duncan

BRITISH TUBERCULOSIS ASS. **Chronic Bronchitis Subcommittee. Chemotherapy in Chronic Bronchitis. Influence of Daily Penicillin and Tetracycline on Exacerbations and their Cost.** A Report to the Research Committee prepared by R. S. FRANCIS & C. C. SPICER. *Brit. Med. J.* 1960, Jan. 30, 297–303. [15 refs.]

Between June 1955 and June 1956 bronchitis caused the loss of 22 million working days among men in England and Wales. Previous work has suggested that antibiotic treatment is of value in this condition [this *Bulletin*, 1959, v. 34, 22; 1960, v. 35, 333]; this investigation by the Research Committee of the British Tuberculosis Association Chronic Bronchitis Subcommittee was undertaken because previous trials had been based on small numbers, and secondly the high cost of tetracycline compounds suggested that the value of penicillin should be tested as a possible alternative.

A double blind control trial was undertaken at 16 chest clinics. These produced 252 suitable patients who were allotted at random to 3 groups receiving: (1) tetracycline 250 mgm. twice daily in capsules; (2) penicillin V 312 mgm. twice daily in capsules: equivalent to 1 million units daily; (3) inert (starch) capsules twice daily. Treatment was started on January 5th, and ceased on April 30th, 1959. Information recorded was as to the number and duration of "bronchitic exacerbations and pneumonic episodes", the average number of working days lost, and the money lost to the patient through time off work and to the State from sickness benefit.

A full survey of sputum bacteriology was not considered practicable. The criteria by which patients were selected for the trial is detailed together with the points in organization. Evidence is given that the allocation of patients to each group was even and fair.

Of the 252 patients enrolled in the trial 26 were excluded; the remaining 226 cases fell into 2 categories. 185 were continuously under observation, and at risk during the trial, and 41 were only intermittently at risk because they entered the trial late owing to previous illness, etc. Analysis of the 226 cases showed that both penicillin and tetracycline were beneficial in reducing the days off work due to bronchitic exacerbations or pneumonic episodes. The average days off work per man day under observation in the 3 treatment groups were: 0·066 penicillin, 0·084 tetracycline and 0·171 control. It appears, therefore, that both antibiotics approximately halved the time off work, but did not differ significantly from each other.

Separate analysis of the 185 cases under observation continuously throughout the trial, showed that the benefits of antibiotic treatment are equally evident in this group, but the apparent superiority of penicillin over tetracycline disappears. The approximately equal efficiency of penicillin and tetracycline is an unexpected finding, since the former is considered to have little effect on organisms of the *Haemophilus* group.

The treatments appear to have no effect in reducing

the number of attacks per patient. The average number of attacks were as follows: penicillin 0·92; tetracycline 1·07; control 1·04.

When the average amount of money lost is added to the cost of the drugs the penicillin group showed a net cost of £30, tetracycline £50, and control £40.

The unexpected result that penicillin seemed to be as efficient as tetracycline was possibly due to the dose of tetracycline being inadequate to inhibit more than an occasional strain of *H. influenzae*.

This is a very interesting research; the findings may be considered as authoritative, but as the authors point out, are only applicable to the conditions under which the trial took place. *F. H. Young*

MURDOCH, J. McC., LECKIE, W. J. H., DOWNIE, Jean, SWAIN, R. H. A. & GOULD, J. C. **An Evaluation of Continuous Antibiotic Therapy in Chronic Bronchitis.** *Brit. Med. J.* 1959, Dec. 12, 1277–85, 2 figs. [41 refs.]

This paper reports 2 double blind trials of continuous daily tetracycline/oleandomycin and oxytetracycline treatment in patients with chronic bronchitis, carried out during the winters of 1957–8 and 1958–9 respectively. 23 patients were observed in the first trial, and 75 including 20 from the former trial were seen in the second. The methods adopted are described in detail.

In the first trial Sigmamycin (167 mgm. of tetracycline and 83 mgm. of oleandomycin in each capsule) was used 4 times daily from January 1st to March 31st. 12 patients received the treatment, 11 patients had blank capsules. In the second trial 35 of 75 patients took one 250 mgm. capsule of oxytetracycline 4 times daily, from October 1st 1958 to March 31st 1959, and 40 were given blank capsules. During both winters the assessment of each patient was based on the subjective and objective findings entered at each fortnightly interview. They were recorded as improved, unchanged or worse. The development of side effects severe enough to cause the patient distress was considered a failure of treatment. Details of the bacteriology of the organisms counted in the sputum is given.

In the first trial 11 of the 12 patients who received the active preparation were clinically improved, and 1 remained unchanged. By contrast only 1 of the 11 patients who received the inactive preparation was clinically improved while the remainder got worse. 10 out of the 12 patients receiving active treatment lost no days of work, whereas of the 11 receiving the inactive capsules only 2 came into this category. Bacteriologically, both *Haemophilus influenzae* and the pneumococcus were isolated much more frequently in those who were to receive active treatment. *Staph. aureus* was isolated with a significantly higher frequency in the sputum of those receiving active treatment.

In the second trial 35 patients were receiving active treatment, 26 completed the course; 23 were improved, 2 were worse, and 1 failed treatment because of persistent nausea, and 9 were withdrawn for a variety of reasons. 22 patients did not lose any days from work; of the 40 patients receiving inactive treatment, only 19 completed the course, and they were all clinically unchanged, though 10 felt better in themselves. 13 of the 19 patients who completed the course lost no days from work.

There was good correlation at any time between the clinical state of the patient and the degree of purulence of the sputum, presence or otherwise of *H. influenzae*, or the pneumococcus or both.

The authors point out that there is considerable danger of superinfection with staphylococci in patients who have been admitted to hospital with exacerbations of bronchitis. The degree of purulence of the sputum is a useful guide to the efficiency of antibiotic treatment, since there is a good correlation between it and the clinical state of the patient and the presence of *H. influenzae* and pneumococcus. To obtain a reliable report the doctor himself should examine the sputum to be classified as purulent or non-purulent. Gross disturbance of the normal surface flora of the respiratory and intestinal tract was not evident. Owing to the possibility of superinfection with staphylococci it is thought that treatment should be carried out by the general practitioner at home, and if possible the patient kept away from hospital. The cost of continuous treatment with oxytetracycline in a dose of 1 gm. daily for 6 months is £63 14s. in general practice.

This well conducted experiment lends weight to the theory that in severe cases of bronchitis continuous oxytetracycline during the whole winter is very useful. *F. H. Young*

MAYNARD, E. P., Jr. & GROVER, V. **The Effect of Childbearing on the Course of Rheumatic Heart Disease: a 25-Year Study.** *Ann. Intern. Med.* 1960, Jan., v. 52, No. 1, 163–71.

The study described in this paper was undertaken to attempt to shed light on the problem of the ultimate effect of childbearing on the course of rheumatic heart disease. Records of 455 women were available and 97·4% of these women were studied by the same group of physicians in an intensive follow-up during a period of 25 years. A preliminary report was presented in 1954 but critical analysis "revealed biases which were not recognized at the beginning". The actual results of the study were therefore not published at that time but are now presented as the authors consider that the "clinical impressions" then obtained and a description of the difficulties encountered in the statistical analysis of the data may be of value to other investigators.

The method adopted for the study of the "records of all female patients with rheumatic heart disease treated in the adult cardiac clinic of the Brooklyn Hospital from its inception in 1924 through the year 1948" is described. There are tables and description of results which in summary "show that (1) women who were non-parous at first observation had a poorer survival rate than did the parous, and the most favourable survival rates were exhibited by women who had had two or more full term pregnancies prior to first observation; and (2) women who had subsequent children within five years after the first observation had much better survival rates than did women who did not become pregnant after the first observation". It is

clear that the selective effect of the factor of rheumatic heart disease which is under study creates a natural bias as, for example, "the more favourable experience of the parous woman probably results from a tendency of the nonparous not to become pregnant". The statements are made that "this type of study cannot give us more than a clinical impression" and "there is certainly no evidence that pregnancy has a long-term detrimental effect in a large group" and "Individually, pregnancy must be looked upon as a temporary hurdle, and each case must be considered individually".

M. E. Delafield

CANCER

STOCKS, P. **Cancer Registration and Studies of Incidence by Surveys.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 4, 697–715. [13 refs.]

An account is given of the cancer registration schemes which exist in Belgium, Canada, England and Wales, Denmark, Finland, France, Holland, Iceland, Japan, Norway, Sweden and the U.S.A. and the information collected by each registry is specified. Different systems are used for allocating the year in which the cancer is regarded as having occurred. This will not affect comparisons between crude annual morbidity rates, but it will affect comparisons between age-specific rates as these will be different according to whether the cancer is allocated to the year of registration or the year of onset of symptoms. Data for cancer of different sites registered in England and Wales show a fairly constant lag of 6 months between onset of symptoms and registration for all sites in both sexes—the range of difference being between 3·7 months for cancer of the intestine in men and 9·2 months for epithelioma of skin in women. The rates will also be affected by the proportion of cases which are registered only as a result of death certification. Data from 4 registries show that this ranged between 10% and 36% of all cancer registrations; it has tended to fall the longer the registry has been established. It is suggested that the age at onset of symptoms is the most suitable age to use for the purpose of calculating age-specific morbidity rates.

A method of standardizing for age is suggested, which will enable international comparisons to be made effectively and simply. The numbers of persons aged 35–44 years, 45–54 years, 55–67 years, 65–74 years, and 75 years and over, in England and Wales, Scandinavia and the U.S.A. are almost in the ratio of 5:4:3:2:1 and a standardized rate for persons over 35 years of age can be obtained by multiplying the age-specific rates at these ages by 5, 4, 3, 2 and 1 respectively. To include persons aged under 35, the rate under 35 years of age can be given a weight of 0·55 and the standardized rate at 35 years and over can be given a weight of 0·45.

Incidence rates at ages 0–34 years and age-specific rates at ages over 35 years expressed as percentages of the standardized rate at 35 years and over are given for cancer of 10 sites in 10 parts of the world.

[In Table 6, rates per 100,000 appear to have been given instead of percentages in a few instances and there are a number of misprints. It is advisable to check the figures before making use of them.]

Richard Doll

SELTZER, C. C. **Masculinity and Smoking.** *Science.* 1959, Dec. 18, v. 130, 1706–7.

A study has been made of 252 Harvard College sophomores first seen between 1938 and 1942 and "selected for their lack of visible abnormality". Their smoking habits were recorded then and through subsequent annual questionnaires and on this basis they can be classified as non-smokers (60), moderate smokers (94) and heavier smokers (93). [There is no explanation of the missing 5.] From the initial examination each man can also be classified in terms of masculinity as indicated by external morphological features. Tabulation in relation to these two features shows that a "strong masculine component" was present in 97% of the non-smokers, 90% of the moderate smokers and 83% of the heavier smokers. At the other end of the scale the more feminine build was the feature of no non-smokers, 2% of moderate smokers and nearly 9% of heavier smokers. These persons with weakness of the masculine component have a characteristic pattern of traits which includes an aversion for strenuous exercise and sports and low physical fitness for hard muscular work; they are less well integrated and more ideational, creative and intuitive.

[It would seem that the rugged "he-man" of the cigarette advertisements is due for replacement.]

A. Bradford Hill

See also p. 418, HORN, COURTS, TAYLOR & SOLOMON, **Cigarette Smoking among High School Students.**

SHANTA, V. & KRISHNAMURTHI, S. **A Study of Aetiological Factors in Oral Squamous Cell Carcinoma.** *Brit. J. Cancer.* 1959, Sept., v. 13, No. 3, 381–8.

Oro-pharyngeal carcinomas constitute 48% of all cancers seen at the Cancer Institute, Madras. In a search for an explanation of this situation comparison has been made of 206 persons with squamous cell carcinomas of the cheek or floor of the mouth with a random control group of 278 persons without cancer. With carcinoma of the cheek the outstanding difference between the 2 groups was the habit of betel, nut and tobacco chewing which was found in 85% of the cases against only 12% of the controls. This compares with 9% and 52% respectively who chewed pure betel and nut *without* tobacco. Associated with the tobacco there was also an abnormally high incidence of dental sepsis in the carcinoma group, which appears to promote the

carcinogenic action. With cancer of the tongue (71 cases) this habit of betel, nut and tobacco chewing was again significantly frequent, particularly for the anterior two-thirds. It may be concluded, therefore, that combined tobacco, betel and nut chewing over 15–20 years, together with the oral sepsis thus produced, is the most important factor in the remarkedly high frequency of oral carcinomas. *A. Bradford Hill*

MISCELLANEOUS DISEASES

VAN DEN BERG, B. J. Ongevallensterfte in Nederland in het bijzonder bij kinderen tegen de achtergrond van het ongevallenvraagstuk in het algemeen. **[Accident Mortality in the Netherlands especially among Children against the Background of the Accident Problem in General]** pp. xiii + 162, 22 figs. [Numerous refs.] 1959. English summary. Leiden: Nederlands Instituut voor Praeventieve Geneeskunde, Wassenaarseweg 56.

This is a detailed analytical survey of the present accident problem in the Netherlands. There is a good summary in English and the headings of the numerous tables and figures are also translated. There are 10 chapters which in addition to the introduction present information on accident mortality in general, accidents in children, transport accidents, drowning, home accidents, suicide, other accidents and socio-medical aspects of accident prevention.

In the Netherlands 4,600 die annually as a result of accidents. This mortality is analysed by age and sex. There are peaks of mortality in preschool children (35 per 100,000), the male 20–29 age group (45) and in aged persons (100). The total number of deaths due to accident is 1,000 in the under-20 age-group which represents about 35% of the mortality at this age whereas 50 years ago the proportion of accidental deaths was only 7%. There is a good discussion of accident mortality in children. Recent mortality figures (1955–57) indicate that of 1,000 boys born, 35–40 will die before their twentieth birthday and of these deaths 6–7 will have been through accident. The respective figures for girls are calculated at 25–30 deaths of which 2–3 are from accident.

Road traffic accident deaths were about 1,700 annually in 1955–57 but this toll has diminished since 1958. Among other points to which attention is drawn are the high mortality from drowning in the Netherlands as compared with other countries; the high proportion of home accidents and the need for better construction of houses and of household utensils and the need for modernization of heating and cooking apparatus, since coal-gas causes a considerable number of poisonings. Burns and scalds cause about 100 deaths annually and falls cause 1,000 deaths per annum and of these 800 are in old people. Suicide deaths number about 400 in men and 250 in women; the suicide rates in the course of the century have decreased only slowly for men and have slightly increased for older women.

The different aspects of accident prevention are described. *M. E. Delafield*

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Atmospheric Pollution; Port, Ship and Aviation Hygiene; Infestation.**

GENERAL

UNITED STATES PUB. HEALTH SERVICE. **Conference on "Man versus Environment", May 5–6, 1958.** Proceedings edited by H. A. FABER, assisted by Marie H. PEAK. 143 pp. 1959, Jan.

This publication contains the papers and their discussions presented at a Conference on "Man versus Environment" which was sponsored by the National Institutes of Health and Bureau of State Services of the United States Public Health Service. Its foreword states "The concept of a conference to delineate new and complex problems in the field of environmental health was proposed by Dr. Henry F. VAUGHAN, Chairman of the Sanitary Engineering and Occupational Health Study Section of the National Institutes of Health.

"It was intended that the conference should emphasize the need for greater concentration upon research, planning, programming, and evaluation in order to control these problems".

In the papers attention was focussed on the problems resulting from new developments in science and technology in the major fields of: water supply (2 papers), water pollution (2 papers), air pollution (2 papers), food technology (2 papers) and occupational health.

In an *Introductory Statement* (pp. 1–3) Henry F. VAUGHAN spoke in general terms of the problems brought about by progress. Some of these are old

problems with new facets but others, which include those of radiobiology and the use of atomic energy, remain largely unexplored.

There followed a Keynote Address entitled *Human Health and the Modern Environment* (pp. 5–14) by Robert A. KEHOE in which there is an able review of many of the practical health problems of the present day with particular discussion of those which exist in an industrial society. "It must become an axiom of modern chemical and technologic research that the materials produced and the forms of energy harnessed must be as well understood for their biological potentialities as for their physical and mechanical properties."

WATER SUPPLY PROBLEMS

(1) *Research Problems in Water Supply* by Harry E. JORDAN (pp. 15–21). Among the problems which are shortly described in this paper are those arising from: (1) the low water resources potential of Australia, (2) the necessity for water storage and conservation in parts of the United States arising from increase in population and increased *per caput* use of water, (3) the possible transmission of virus infections by water about which adequate information is lacking, and (4) the new chemical water contaminants—the detergents and the tremendous number of insecticides which, used to protect fruit and vegetables, ultimately find their way into surface or ground water and may perhaps have a chronic toxic action on the body even when ingested in small amounts.

(2) *Water Supply Research* by M. D. HOLLIS (pp. 23–30). In this paper there are comments and brief descriptions of research needs in water supply and the need for the evaluation of research under the headings of: (1) water supply augmentation from converted seawater and from atmospheric moisture, (2) conservation, (3) recharge, (4) reduction of evaporation, (5) organic substances in water—their nature, source and toxicity, (6) removal of particulate matter and (7) viruses in water.

WATER POLLUTION PROBLEMS

(1) *Water Pollution—the Scope of Research Needs* by J. E. MCKEE (pp. 31–37). In this paper there is a discussion of traditional patterns for water pollution abatement, the nature of fundamental and applied research and of the present needs of specific research into particular problems. Appended to the paper are abstracts (pp. 38–48) from various sources on research problems in need of study in which there are lists of suggestions and of priority selection.

(2) *Water Pollution—Practical Aspects of Research Needs* by Ralph E. FUHRMAN (pp. 49–57). This is a short paper on the need to support research and the need of qualified personnel to conduct it. The author added to the lists of needed researches mentioned in the previous paper some further suggestions for research on odour control and for securing higher waste-water effluent standards.

AIR POLLUTION PROBLEMS

(1) *Research Problems in Air Pollution* by Louis C. MCCABE (pp. 59–64). This paper contains a general discussion of some of the research problems on air pollution which exist to-day for "The explosion of world population, the expansion of communities and the growth of industry are accompanied by increases of air-borne wastes, new kinds of pollution or well-known contamination released in new places". The economic effects of air pollution are more readily appraised than are health effects about which scientific evidence is at present lacking especially in respect of the influence of long-time exposure to small amounts of contamination.

(2) *Future Problems in Air Pollution Research* by Leslie A. CHAMBERS (pp. 65–72). In this paper the author described some of the chemistry of air pollution and the problems connected therewith. There followed "speculation on what may constitute the major air pollution concerns of the next half century" under the headings (1) pollution by radioactive materials, (2) meteorological control of local air pollution, (3) the effects of air pollution on world climate and (4) "jurisdictional" problems in air pollution control.

FOOD TECHNOLOGY PROBLEMS

(1) *Research Problems in Food Technology* by Emil M. MRAK (pp. 73–80). "Food technology is a relatively new field involving the application of various natural sciences and of engineering to the handling, processing and distribution of foods." This is a development which has resulted to a large extent from "great changes occurring in the eating habits of the American people". Processing of food has its problems which are shortly reviewed in this paper and arise in "the factors of color, flavor, texture, convenience, stability, asthetics, nutrition and safety all of which influence the consumer". There is need for research also to study certain aspects of changes in food brought about in dehydration and low temperature preservation.

(2) *Problems in Food Technology Research* by Walter D. TIEDEMAN (pp. 81–85). This is a short paper in which mention is made of the need for research in subjects such as: (1) coin-operated vending machines for hot dinners which are only "just around the corner", (2) sterilization of food by radiation and (3) food poisoning and the "possible role of foods in spreading virus diseases".

OCCUPATIONAL HEALTH PROBLEMS

Research Problems in Occupational Health by James H. STERNER (pp. 87–94). The needs of research in occupational health are considered in general terms in this short paper. The problems are discussed in the 3 categories: (1) Man and hazardous chemical and physical agents, (2) Man and machine, and (3) Man and Men.

There are good reports of the group discussions which followed the papers.

There is an excellent "Summary Statement" of the proceedings of the Conference and its recommendations by Abel WOLMAN (*Man in a Complex Environment*, pp. 131-136) in which there is the statement "Out of the deliberations of this Conference comes not a poverty of ideas, but a surfeit of riches in variety and detail. In that very detail lies a great deal of our problem of analyzing a new kind of objective. The objective is familiar: to go through this forest of suggested rich ideas and emerge with a purposeful program".

An appendix gives a list of over 80 participants in the Conference. *M. E. Delafield*

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

WAGNER, Edmund G. & LANOIX, J. N. **Water Supply for Rural Areas and Small Communities.** *World Health Organization Monograph Series No. 42.* 337 pp., 85 figs. 1959. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [35s.; $6.75; Sw.fr. 20.–.]

This is a textbook on water supply. It is written by two American public health engineers and will be found useful by many American public health engineers.

It begins, as do all textbooks on water supply, by inviting us to imagine life without water; by recalling the popularity of this fluid "since the dawn of history"; by reminding us that all biological life is dependent on water and by warning us of its death-dealing as opposed to its life-giving properties. "The history of public health is filled with both tragic and glorious milestones in which water was the important factor."

It is a comprehensive textbook. Its chapters range from *Objectives and Concepts* to *Administration and Finance*, but much of the information in the intervening chapters is excellent and relative to the problem of water supplies in the tropics. The chapter on *Ground Water* is particularly good and the technical details on the improvement of existing wells have the great merit of clarity. The notes on the household purification are first class but could be expanded with advantage. Purification by the householder is the only system of purification in a very large part of the tropics, and one may question whether it can be adequately dealt with in the space of 8 pages in a volume which runs to 340 pages.

It is a well illustrated textbook. There are no less than 85 illustrations, and 9 annexes (for the benefit of the English speaking world an "annex" is a P.S. and may be merely a list of conversion tables (annex 2) or an excellent chapter on the construction of hand-dug wells (annex 5).

If there is a need for another textbook on water supply, this book fulfils that need. Even if the need be doubted this work deserves a place in every library which seeks to maintain a comprehensive section on water supplies.

But is the writing of textbooks the proper function of the World Health Organization? This volume is the 42nd WHO Monograph and the subjects dealt with have ranged from the psychiatric aspects of juvenile delinquency to the disposal of sewage. These volumes vary as much in their method of approach and their literary merit as in their range of subjects. Has the time not come when one may reasonably ask what sort of publication WHO should issue? To whom should it be addressed? Can it fulfil a need not met by existing textbooks and journals? Should these Monographs have a definite aim, and if so what?

The World Health Organization have many competent field workers especially in the developing countries and it would be a pity if they did not publish their findings. Would not a simple factual description of their public health problems be helpful? A well written account of diseases conquered would be encouraging, and a volume contrasting public health issues in different countries could be illuminating. There are other possibilities which might be considered, but the writing of textbooks should not have a high priority.

G. Graham Don

BUCZOWSKA, Zofia. **Research on the Bacteriological Pollution of Coastal Waters.** *Bull. Inst. Marit. Med. Gdańsk.* 1959, v. 10, Nos. 3/4, 141–50, plan. [15 refs.]

This study of the contamination of in-shore waters with coliform and salmonella organisms adjacent to popular bathing beaches in Poland is of particular interest in view of the recent publication of the report by the Committee on Bathing Beach Contamination of the Public Health Laboratory Service [this *Bulletin*, 1960, v. 35, July]. This report refers to a much more extensive survey of coastal bathing waters in England and Wales than in the article under review, where the sampling points were all in the Gulf of Gdańsk in Poland. In general, however, the conclusions are of the same order: in spite of the pollution of coastal bathing waters with faecal coli and salmonella organisms there was little evidence to show that these contaminated waters constituted a health danger to bathers. In both cases the salmonella isolation rate showed a relation to the coliform counts and *Salmonella paratyphi B* was the most frequent serotype isolated. In the Polish study it is indicated that the distribution of the salmonella serotypes isolated from the bathing waters was in agreement with the sickness and carrier records of the areas involved, but no details are given and no examples quoted of infections contracted by persons bathing in these contaminated waters. *H. J. Bensted*

CROFT, C. C. **A Comparative Study of Media for detection of Enterococci in Water.** *Amer. J. Public Health.* 1959, Oct., v. 49, No. 10, 1379–87. [1[illegible] refs.]

ROTHE's azide dextrose broth (AD) [this *Bulletin*, 1951, v. 26, 278] was compared with Hajna's buffered azide glycerol broth (BAGG) in multiple tubes and with SLANETZ and BARTLEY's M-enterococcus agar with membrane filters (MF) [*ibid.*, 1958, v. 33, 495] for enumeration of enterococci in water. A proportion of samples was also examined by Kereluk's ethyl violet azide agar (K-EVA) with membrane filters. Confirmation in ethyl violet azide broth (EVA) [*ibid.*, 1953, v. 28, 1077] was made on all presumptive positive tubes and a selection of colonies from membranes. Positive results in the EVA medium were considered to indicate enterococci according to the SHERMAN criteria [*ibid.*, 1938, v. 13, 481] in 98% of cases [*ibid.*, 1954, v. 29, 181].

Eight laboratories examined 185 samples. All cultures were incubated 48 hours at 35°C.

AD-EVA gave results in close agreement with MF and both gave significantly higher results than BAGG-EVA. The K-EVA medium gave lower results and smaller colonies than MF on the 29 samples examined. Ratios of enterococcus to coliform densities ranged from 11·0 to 0·001. Median ratios of coliforms to enterococci for flowing water, impounded water, wells and sewage were 5:1, 4:1, 2·5:1 and 10:1 respectively.

E. Windle Taylor

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

KELLER, P. **Bacteriological Aspects of Sewage Purification and River Pollution.** *J. Hygiene.* 1959, Dec., v. 57, No. 4, 410–26, 2 figs.

"Rapid industrial development in South Africa has resulted in an increasing demand for water for all purposes. Consequently it has become urgent to consider the role of purified sewage and industrial effluents in the conservation of water supplies."

The experimental work described at considerable length in this paper consisted in the bacteriological study, by methods which are detailed, of the effect on bacterial populations of:—(1) conventional sewage treatment (biological filtration, humus tank sedimentation, sand filtration and activated sludge treatment), and (2) further biological purification by vegetation ponds or *vleis* (ponds with a dense growth of vegetation), algal beds, grass-plots, model rivers and maturation ponds. Over a period of 4 years more than 2,500 samples were analysed and "more than 13,000 results are now available for presentation and discussion". There are a number of detailed tables of results and a long summary. Conventional sewage treatment up to the sand-filter stage reduces the number of *Escherichia coli* by more than 99% but as between the humus tank effluent and the succeeding sand-filter effluent the percentage reduction is in general very much less than this and sand-filter effluents were found to contain between 200 and 5,000 *E. coli* per ml. Of the new ways of treating sewage effluents for final discharge into streams artificial *vleis* were found to be far more efficient than sand-filters and best of all were maturation ponds the effluents of which contained only between 1 and 10 organisms per ml. From the results of investigation of the newer methods "it appears perfectly feasible to consider the suitability of effectively purified sewage effluents as sources for raw water supplies for industrial and domestic use".

M. E. Delafield

ATMOSPHERIC POLLUTION

KATZ, M., RENNIE, R. P. & JEGIER, Z. **Air Pollution Hazards from Diesel Locomotive Traffic in a Railway Tunnel.** *Arch. Indust. Health.* Chicago. 1959, Dec., v. 20, No. 6, 493–504, 3 figs. [26 refs.]

The authors describe experiments carried out in Canada in a single-track railway tunnel 6,032 feet long and 20 ft. 6 inches in diameter. The aim was to find out the pollution produced by fully dieselized traffic, before replacing electric by diesel traction. The pollutants measured were carbon dioxide, carbon monoxide, total oxides of nitrogen, nitrogen dioxide, formaldehyde, sulphur dioxide, smoke and particulate matter. Oxygen, and also air flow, were measured, and everyone stationed in the tunnel was under close medical supervision. The only ventilation was that due to the trains themselves which was, however, considerable, as the frontal area of the engines was about half the cross-section of the tunnel.

Apart from two exceptional values obtained from snap samples, carbon monoxide concentration was low whether measured by snap sample, or continuously, or estimated from carboxyhaemoglobin of subjects manning the sampling stations. Concentrations of total oxides of nitrogen, of nitrogen dioxide, and of formaldehyde, however, were high. Carbon and sulphur dioxides were low and there was no oxygen deficiency, but smoke and particulates were high compared with normal urban air. All results are clearly tabulated.

The only medical findings were minor eye and throat irritation on three occasions, and no toxic after-effects were detected.

The results are discussed, and reasons for recommending forced ventilation are given.

John McK. Ellison

METTIER, S. R., Jr., BOYER, H. K., HINE, C. H. & MCEWEN, W. K. **A Study of the Effects of Air Pollutants on the Eye.** *Arch. Indust. Health.* Chicago. 1960, Jan., v. 21, No. 1, 1–6. [28 refs.]

"Rabbits were exposed to acreolin (2 ppm), ozone (2 ppm), sulfur dioxide (10 ppm), and nitrogen dioxide (20 ppm) acutely and chronically.

"The ophthalmologic and biochemical effects of these gases on intact and deepithelialized corneas were assayed. Under these conditions no effects were noticeable.

"The effect of these gases and presumably smog in general is at a lower subjective sensory level."

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

KEHOE, R. A. **A New Look at Preventive Medicine in American Industry.** *J. Amer. Med. Ass.* 1960, Jan. 30, v. 172, No. 5, 435–8.

In this interesting and authoritative article the author says "Medicine in American industry has acquired a greatly improved status in recent years and one which holds great promise, not only for its own future development but also for the fulfillment of the growing responsibilities of medicine generally, within a society that has surrounded itself with a multitude of new and artificial dangers to life and health in its headlong technological pursuits". Nevertheless, "we have not learned enough" of the "potentialities for harm that lie in the impact of technology and industry on man", and attempts should be made to secure that medical knowledge and practice should keep abreast, as far as possible, with changing social conditions. In this connexion there is discussion of 3 features of the situation. Research in occupational medicine has hitherto been focused largely on toxicology and environmental engineering. Much valuable work has been done in these fields and this work will continue but in the present situation "the chief goals of industrial medical research are the elucidation of physiological mechanisms and the development of useful clinical and statistical procedures for the recognition of such mechanisms in action". The second point which is discussed is education in occupational medicine, which at present is not adequate either at undergraduate or graduate level in giving attention to the problems of industry in a complex industrial society. Finally the subject of occupational medicine as a specialty is discussed with mention of the recognition of occupational medicine by affiliation with the American Board of Preventive Medicine. *M. E. Delafield*

PATTY, Frank A. **Industrial Hygiene and Toxicology. Vol. I. General Principles.**

This book was reviewed in this *Bulletin*, 1959, v. 34, 1311.

ASHFORD, J. R. **A Problem of Subjective Classification in Industrial Medicine.** *Applied Statistics.* 1959, Nov., v. 8, No. 3, 168–85, 4 figs.

PUGH, D. S., GORDON, C. & LÉVY, Katherine. **Sickness Absence among Railway Clerical Staff.** *Brit. J. Indust. Med.* 1959, Oct., v. 16, No. 4, 269–73, 1 fig.

The sickness experience of railway clerical staffs in Scotland has been analysed in quinquennium age-groups from 45 to 64 for 3 grades of workers, 177 chief clerks, 391 senior clerks and 692 clerks. A progression existed between the grades and the amount of sickness and the number of attacks. The annual number of days lost was 7·1 for chief clerks, 10·7 for senior clerks and 13·1 for clerks and the episode rate was 52, 58 and 65 respectively. The chief clerks had more short time sickness than the other grades. Sickness absence showed a marked increase with age except at ages 60–64. At age 60–64 the chief clerks had less than one half of the sickness in the preceding age-group and the senior clerks had a small fall while the clerks showed only a small rise. The gradient between the groups was due to 6 categories of sickness—functional nervous disorders, bronchitis, disease of the circulatory system, diseases of the stomach and duodenum, accidents and diseases of bones and organs of movement. The percentage of the total days of sickness due to these groups of causes was 32 for chief clerks, 49 for senior clerks and 58 for clerks. There was no definite gradient between the 3 groups of workers for the remaining causes of sickness absence. The results were compared with those from London Transport Clerical and Technical Staff. The attack rate among the railway workers was lower than among the Transport staff and the average duration of attack was longer but in general the pattern of sickness was similar.

[For an earlier study, see this *Bulletin*, 1959, v. 34, 1258.] *W. J. Martin*

STÝBLOVÁ, V. Neurologische Erscheinungen bei Werktätigen, die Vibrationen ausgesetzt sind. [**Neurological Conditions in Workers exposed to Vibration**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 5, 485–503. [Numerous refs.]

The observations reported in this paper are preceded by references to the literature on the clinical conditions which may be caused in workers by exposure to vibrations with mention of the various occupations in which workers are exposed to vibrations of greatly varying frequency and amplitude.

In a period of 4 years a total of 350 workers were observed. This number was composed of groups of men, such as riveters and plate workers, who used pneumatic tools, and others who were exposed to finer vibrations in grinding files and glass. This neurological investigation was restricted to those types of worker in whom the upper extremities are mainly exposed to vibration. There is a full description of the clinical findings with tables and discussion. Subjective neurological symptoms occurred in 65% of the workers in

aggregate. For example, among riveters, 104 person in all, the symptoms of blanching of fingers were noted in 76%. Other symptoms in the upper extremities were paraesthesias (85%), pains (49%) and cramps (13%). In general these symptoms were not severe but evidence of marked organic changes in the nervous system such as a polyneuritic syndrome and amyotrophic lateral sclerosis was found in 9% of the workers. The prophylaxis and treatment of the neurological effects of exposure to vibration are discussed.

M. E. Delafield

MINISTRY OF LABOUR & NATIONAL SERVICE. H.M. FACTORY INSPECTORATE. **Safety in the Use of Abrasive Wheels.** *Safety, Health & Welfare, n.s. No. 4.* 64 pp., numerous figs. 1959, Aug. London: H.M. Stationery Office. [4s.]

This booklet is intended to advise on precautions for the prevention of accidents in the use of abrasive wheels. The risk of a breakage is inherent in every such wheel, and if the frequency of breakage is to be kept low the initial care exercised by the makers of wheels and machines must be coupled with the adoption of sound safety measures by the users. Most of the accidents due to wheel breakages could have been avoided by an appreciation of the risks and of the safety precautions necessary.

The booklet deals with the risk of injury resulting from wheel breakage, contact with the running wheel, and projection of the work. For information on other important health and safety requirements (*e.g.*, the removal of dust) the reader is referred to the Factories Acts and various Regulations.

A section on safety in grinding operations deals with the breaking of wheels; examination, handling and storage of wheels; selection of a wheel; wheel speeds, and the factor of safety. It is imperative that the maximum permissible wheel speed stated by the maker should not be exceeded. In another section in which the grinding machine is discussed it is emphasized that an abrasive wheel should be mounted on the type of machine for which it is intended, and never on makeshift apparatus. Speed control, work rests, and magnetic tables are also discussed. A further section is devoted to methods of mounting wheels, and detailed precautions are outlined.

Under the heading *Protection against bursts* the importance of wheel guards is stressed. These should always be used (1) to contain the wheel parts in the event of a burst; (2) to protect the wheel against inadvertent damage; (3) to prevent, as far as possible, the operator coming into contact with the wheel; and (4) to prevent an oversize wheel being fitted. Another section on the operation of abrasive wheels gives advice on the truing and dressing of wheels, wheel balance, grinding solutions, protection of the eyes, and the grinding of magnesium alloys.

Further sections of the booklet deal with portable grinders, mounted wheels and points, and abrasive cutting-off wheels; and there is a useful summary of operating precautions.

Thomas Bedford

(3276)

MINISTRY OF LABOUR & NATIONAL SERVICE. H.M. FACTORY INSPECTORATE. **Cloakroom Accommodation and Washing Facilities in Factories.** *Safety, Health & Welfare, n.s. No. 5.* 33 pp., 21 figs. 1959, Mar. London: H.M. Stationery Office. [2s. 6d.]

"The provision of adequate cloakroom accommodation for clothing not worn during working hours is required by the Factories Act, 1937, to be made for employed persons in industry. The Act also requires the provision and maintenance of suitable facilities for washing."

This is an excellent booklet, the aim of which is to enlarge on these legal requirements, to give guidance and to suggest improvements on the minimum requirements. It is well produced and clearly written with a considerable number of excellent illustrative figures. There are 3 appendices which give the dates and numbers of the relevant special regulations and welfare orders.

Additional information and an advisory service are available to employers and others at the Industrial Health and Safety Centre, Horseferry Road, Westminster, London, S.W.1.

M. E. Delafield

STEELE, E. C. **Rehabilitation Program in Ontario for Occupational Injuries.** [Report to the Committee on Rehabilitation (DE FOREST, R. E., Secretary).] *J. Amer. Med. Ass.* 1960, Jan. 9, v. 172, No. 2, 163–7, 4 figs.

Administrative powers, not necessarily limited to legal precedent, were given to commissioners to interpret the intention of the Compensation Act, primarily designed "to get rid of the nuisance of litigation" and "to have swift justice meted out to the great body of men" who suffer industrial disease or injury. To assist the injured workman to return to his job as quickly as possible, with minimal impairment, a clinical rather than a forensic approach enabled individual doctors to take their part in a team effort. Medical care, physical medicine and vocational and financial rehabilitation were more humane to the injured and less costly to employers.

Initially the patient has choice of doctor who calls for whatever consultant advice and facilities for investigation and treatment are necessary, either locally or centrally in one of the province's teaching hospitals, partly rented by the commissioners. Co-operation between all, practically regardless of cost, and liaison with employers, unions and welfare associations contribute to early rehabilitation.

Physical and occupational therapy, started in a small way in 1932, are now extended locally or in a 550-bed hospital where planned, supervised activity is the keynote. Work-assessment leads to realistic tasks, indoors and outdoors, with tools of the trade when possible. The theory is: rehabilitation always, resettlement sometimes and retraining as infrequently as possible. Retraining, preceded by intelligence, aptitude, experience and personality evaluation, makes use of business colleges, electronics and welding schools, engineering courses, etc. Of 80,000 men injured in 1959, only 91 were retrained. The most difficult to place were un-

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skilled and older workers, those handicapped by head or back injuries or dermatitis, previously disabled persons, seasonal workers and those with unsatisfactory work records.

Treatment and appliances are free, and prompt pay ment during incapacity is an important factor in th successful rehabilitation-compensation process.

M. Patricia Fitzsimons

OCCUPATIONAL DISEASES

FAY, J. W. J. & ASHFORD, J. R. **Size Distribution of Airborne Dust Samples from British Coal-mines.** *Brit. J. Applied Physics.* 1960, Jan., v. 11, No. 1, 1–13, 18 figs. [16 refs.]

In discussing airborne dusts it is useful to be able to specify their particle size distribution by a simple formula, but at present no single formula is generally accepted. In this interesting paper the authors consider several which have been suggested in the United Kingdom and in South Africa and compare them with very extensive determinations of particle size distributions of dusts in British coal-mines.

The dusts from which the data were derived were sampled by thermal precipitator as part of the National Coal Board's Pneumoconiosis Field Research Programme (FAY, *Nature*, 1957, v. 180, 309) and they came from coal faces and elsewhere underground and on the surface at 26 selected collieries throughout coalfields in England, Scotland and Wales. The samples were sized by optical microscope; the particles were divided into the ranges 0·5–1 micron, 1–2·5 microns, 2·5–5 microns and over 5 microns, but owing to the doubts cast on the validity of optical sizing of particles smaller than 1 micron diameter those in this range were only considered in detail for particular purposes. One of these was the study of the origin of these smallest particles; the authors show that at any one mine the number counted smaller than 1 micron varies little between coal-face and surface, supporting the contention that most of such particles are not mine dust but are due to air pollution [CARTWRIGHT and SKIDMORE, this *Bulletin*, 1957, v. 32, 867]. From this the authors very tentatively conclude that since pneumoconiosis is not found among workers who have mainly done non-dusty surface work, particles below 1 micron are of little industrial importance.

In dealing with particles larger than 1 micron 4 postulated size distributions are considered: (1) the negative exponential, chosen because if particles smaller than 1 micron are omitted the distribution suggested by WYNN and DAWES (*Safety in Mines Research Establishment, Res. Rep.*, 28, 1951) reduces it to this; (2) the distribution suggested by SICHEL [this *Bulletin*, 1959, v. 34, 1264], similarly simplified to one term only by omitting particles smaller than 1 micron: Sichel's distribution is identical with that of Wynn and Dawes except that in it the square root of the particle size appears instead of the particle size itself; (3) the power-law distribution proposed by HAMILTON and KNIGHT [*Proceedings of a Conference on the Mechanical Properties of Non-Metallic Brittle Materials*, Paper 21 (London, 1958, Butterworths Scientific Publications]; and (4) a combination of 2 exponential curves, the expression being identical in form to that of Wynn and Dawes, but in which the 2 terms cover the distribution above and below 6 microns respectively. To test each law the logarithm of the observed number of particles per unit size interval was plotted against a suitable function of size, so that if the postulated distribution is correct the plots will be linear. A considerable number of such plots are shown, drawn from various sources, and although no model is completely satisfactory the simple exponential distribution gives as good a fit as the others in most instances; the power law in general predicts too many large particles.

If the exponential distribution is assumed for the above-1 micron component, differences between the particle size distributions of dust clouds will show themselves only in the constant β appearing in the exponent. Study of the variation of β between collieries and between working places shows marked regional differences but only small and random variations within any one mine. Area-size and weight-size distributions are shown for various values of β.

An appendix shows how the size distribution parameter β can be estimated from the counts in the ranges 1–2·5, 2·5–5 and over 5 microns. *John McK. Ellison*

ASHFORD, J. R. **Some Statistical Aspects of Dust Counting.** *Brit. J. Applied Physics.* 1960, Jan., v. 11, No. 1, 13–21, 9 figs.

In this valuable paper the author uses statistical methods to analyse the errors arising in the counting and sizing, by optical microscope, of thermal precipitator samples of airborne dusts. The samples were taken in coalmines, as part of the National Coal Board Pneumoconiosis Field Research programme.

The method of evaluating samples is described and the main sources of error are stated. These are (1) sampling variation in the number of particles within the area counted; (2) the basic error of the counter as indicated by repeated counts of the same traverse by the same counter, due to the difficulty in deciding whether a particle is within a given size-range and of marking off particles counted; and (3) differences between observers. To separate these 3 types of error the logarithms of the numbers of particles counted were used: this is stated to be accepted practice since both variability and personal error increase with the number counted. The logarithm of the number of particles recorded by a given observer at a given time is therefore treated as being the sum of 3 independent terms namely the logarithm of the average count, the logarithm of the observer's error factor at that time and the random error.

The results show that at any given time a particular observer has a characteristic average counting error which with less experienced counters varies with time. By contrast the basic counting error, between repeat counts of the same traverse by the same, experienced, observer, shows little variation between observers continuously engaged in counting slides.

In addition to the errors considered separately the combined errors were studied by analysis of variance. For this different workers counted the same slides but used different traverses. It was found that the coefficient of variation decreases as the number of particles counted increases, as it would if the particles were deposited at random along the length of the deposit and the numbers in different traverses were therefore distributed according to Poisson's distribution, but the coefficient of variation is nearly double that which Poisson's distribution predicts. This difference is discussed.

The basic counting errors arise from (1) failure to count all particles in the appropriate size-range, and counting some twice; and (2) allocating some of those counted to the wrong size-range. Of these the latter is normally the more important, and since the number in a given range normally falls steeply with increasing size this latter can cause overestimates in the count in any range.

The complicating factors of overlapping, contamination, and fall-off of particles are discussed.

John McK. Ellison

LIPPMANN, M. **Review of Cascade Impactors for Particle Size Analysis and a New Calibration for the Casella Cascade Impactor.** *Amer. Indust. Hyg. Ass. J.* 1959, Oct., v. 20, No. 5, 406–16, 6 figs. [19 refs.]

Since the original account of the cascade impactor by MAY [this *Bulletin*, 1946, v. 21, 244] several other instruments for sampling and fractionating aerosols have been described and calibrations published from which particle size distributions are obtainable.

It is convenient to determine the total amount of material upon each of the sampling plates; application of effective droplet sizes (EDS) to the totals then enables a size distribution curve to be reconstructed for the original aerosol without recourse to microscopic counting except, of course, in assigning the EDS values.

The EDS depends upon the jet velocity, V, and the size, D, shape and density, ρ, of the particles. Theoretically, if the particles were spheres, the EDS would depend on ρVD^2 and as long as this group was constant it would be unchanged.

This has been invoked in calibrating different impactors but the geometry of the jets has not always been the same and the mass median diameter (MMD) has been used instead of the EDS. In addition, particles have not been spherical.

3 such calibrations were used to construct size distribution curves for a U_3O_8 aerosol sampled with a Casella cascade impactor and were found to give very different results. Membrane filter size analyses made by optical and electron microscopy gave substantially coarser size distributions than those achieved by applying any of the calibrations to the impactor data.

Certain limitations and errors of impactor technique are discussed and, with these in mind, a modified Casella impactor was subjected to a new calibration procedure with aerosols of materials ranging in density from 1·9 to 10·9. Mass determination and optical sizing of the material on each plate was carried out and simultaneous membrane filter samples were taken. The results are given as diagrams of the stage MMD against particle density. They constitute the best calibration at present available for the instrument but it must be remembered that the effect of varying shape of particle was not examined. *C. N. Davies*

THÜRMER, H. Der Fraktionierungseffekt im Thermalpräzipitator und die Folgerungen für ein elektronenmikroskopisches Koranalysenverfahren. [**Fractionation of Particles in the Thermal Precipitator and its Bearing on Size Analysis by Electron Microscopy**] *Staub.* Düsseldorf. 1960, Jan. 1, v. 20, No. 1, 6–9, 7 figs.

Both theory and experiment indicate that the velocity with which particles move away from a hot surface and towards a cold one is about 3 times greater for sizes which are small compared with the mean free path of air molecules than for large sizes.

If, therefore, the rate of air flow through a thermal precipitator is increased gradually to the stage at which particles begin to pass through the instrument, instead of being deposited, failure in this manner should occur at a lower flow rate for larger particles. This experiment was carried out with coal dust and magnesium oxide smoke by cutting down the heating current through the wire, until penetration commenced, and plotting the critical current against the flow rate of air through the precipitator. It was found that the rate of air flow for magnesium smoke could be increased to about 1·7 times that for coal dust.

The particles deposited on the collection slip of a thermal precipitator are therefore spread out downstream according to size, the coarse ones penetrating the farthest. Curves are shown relating the site of deposition to percentage deposited for 4 groups of radii: <0·19, 0·19–0·50, 0·50–1·5 and >1·5 microns. The first 2 groups show high initial deposition, decreasing downstream and the last 2 show the reverse. The variation is only slight for the group 0·19–0·50 micron but is large for the others.

Although it is easy to avoid errors in counting with the light microscope, because the entire deposit can be traversed, difficulty arises with the electron microscope on account of the small size of the field.

To overcome this a special thermal precipitator was made which had a very thin wire and a narrow gap so as to make the deposit as compact as possible in the direction of air flow; the width obtained was about one-third that of the conventional instrument. The glass slips were coated with a film of carbon which received the deposit and was subsequently floated off onto the gauze of the specimen-holder of the electron microscope so that the deposit ran parallel to the mesh and was located at an aperture, entirely unscreened by

the wires. At a magnification of 2,000 it was possible to cover the whole width of deposit with seven photographs. This technique enables accurate size distributions to be obtained and the variation of particle size across the strip to be demonstrated. *C. N. Davies*

KOSHI, S. **Design of a Portable Photoelectronic Dustiness Meter.** *Bull. Nat. Inst. Indust. Health.* Kawasaki. 1958, No. 1, 26–32, 4 figs. [22 refs.]

Working on the same principal as the Tyndallometer, but employing a photomultiplier cell to measure light scattered by dust particles, this instrument gives a linear relationship between meter reading and dust concentration for dust clouds having a constant distribution of particle size.

Below 10 mgm./m.^{3} of quartz dust smaller than 3 microns the error of observation was greater than with the visual Leitz Tyndallometer but the photocell instrument became increasingly more accurate at high concentrations. In the visual device the scale is non-linear, giving greater sensitivity for small readings. When using either type it must be remembered that the calibration is sensitive to the size and nature of the dust particle. *C. N. Davies*

MORGAN, B. B. & MEYER, E. W. **Multi-Channel Photoelectric Scanning Instrument for Sizing Microscopic Particles.** *J. Sci. Instruments.* 1959, Dec., v. 36, No. 12, 492–501, 4 figs. [10 refs.]

BATTIGELLI, M. La classificazione e la statistica delle pneumoconiosi nell'esperienza del Centro E.N.P.I. presso la Clinica del Lavoro di Milano. [**Classification and Statistics of Pneumoconiosis based on ENPI's Experience of the Pneumoconiosis Research Centre (Clinica del Lavoro), Milan**] *Rass. Med. Indust.* Rome. 1959, July–Aug., v. 28, No. 4, 249–79, 10 figs. [26 refs.] English summary.

The author of this paper is a member of the staff of the Great Industrial Medicine Clinic at Milan and works with the centre set up by ENPI (National Accident Prevention Bureau) for the study and prevention of the pneumoconioses. Here all the X-rays taken by the ENPI mobile units are sent and stored, and since under Italian law all workers in jobs where they may be exposed to the risk of silicosis must have an annual X-ray examination, it will be evident that the numbers must be very large.

The author points out that in view of this the staff of necessity have a great deal of experience in dealing with material which is homogeneous and under standardized conditions.

The report is divided into 4 sections: I. The classification used by the centre. II. The report of the mobile X-ray units for the years 1956–57. III. The prognosis in cases of reticulation or more advanced stages among those exposed to risk in the period 1953–57. IV. The evaluation of the extent of agreement between readings of the X-rays taken at annual examination.

I. The present ENPI classification is as follows: 1. Ac centuated lung markings; 2. "Linear" marking (L and L ii). 3. Reticulation (R i, R ii, and R iii). 4. Micro nodulation (M i, M ii, and M iii). 5. Nodulation (N N ii, and N iii). 6. Coalescing and massive forms (A B, C D). 7. Silico-tuberculosis. This classification i then discussed and compared with the Cardiff-Doua which the author states has rather been influenced b the disease in coal miners, while since means of diag nosis are continually improving so as to show eve "pin-head" lesions, the difficulty of classification ha increased correspondingly.

II. The numbers X-rayed were as follows:—

1956	100,855 exposed to risk	17,752 not expose
1957	113,400 „ „ „	17,522 „ „

The number of cases of silicosis (all forms) foun was:—

1956	2,348 (exposed to risk)	189 not exposed
1957	2,715 „ „ „	271 „ „

35% more workers in the asbestos industry wer X-rayed in 1957 than in 1956, with a 19% increase i the number of cases of silicosis. Here the grea difficulty in the classification of the disease in asbesto workers is emphasized as the various grades ru gradually into one another.

Among industrial personnel, porcelain and ceram workers showed the highest percentage, but the highe percentage of the graver forms of the disease (includin combined tuberculosis) was in the abrasive industrie especially those working with emery, though the autho points out that the numbers are small and thus liab to wide fluctuation. The positive cases in non-ris industries were in persons X-rayed for suspected tube culosis; nearly all were at the reticulation stage an were referable to previous work elsewhere. Taking th 5 industries, mining, steel and iron founding, ste works, and ceramics which together constituted 2/3 o the total numbers and about 70% of the total mediu and advanced silicosis cases the percentage was greate in emery workers and was still rising in 1957.

III. Over the 5 years 1953–57 there has been a co siderable reduction in the incidence of the slight cas in all the major industries but this is not so for th more advanced cases which show a definite rise. Th is probably due to the progression of reticulation other stages, to the examination of patients not se previously, and to improved technique.

For concomitant tuberculosis the extractive industri made the worst showing, in that except for them th percentage "probably active" lessened materially in th quinquennium.

IV. After a long discussion on the value of simu taneous or subsequent reading of the 7 × 7 (cm.) film by 2 persons, or reading by 1 person with and witho using the previous year's X-ray for comparison, th author considers that probably the best way at prese is reading by 1 worker with the previous year's X-ra for comparison.

[This paper deserves to be read in full, but in vie of the 1958 International Conference it would be inte esting to know whether the ENPI classification is be superseded by that proposed at Geneva; see th *Bulletin*, 1960, v. 35, 21]. *W. K. Dunscombe*

LENT, H. & GRAVENKAMP, H. Klinisch-röntgenologische Beurteilung verschiedener Silikose-Formen mit autoptischer Kontrolle. [**Clinico-Radiological Assessment of Silicosis with Autopsy Comparison**] With a foreword by F. BRAUCH. *Beiträge z. Silikose-Forschung.* 1959, No. 62, 1–76, 50 figs. [Numerous refs.]

The authors describe investigations carried out on 142 Ruhr coal miners, in whom an autopsy was performed within two years of clinical assessment. The chest X-rays were re-scrutinized and reclassified in the light of the clinical findings before the morbid anatomy was studied. Eligibility for compensation under the workmen's compensation scheme was considered and errors in awarding compensation are included as mis-diagnoses. The X-rays were finally compared with the lung sections and histological reports. The usual German method of classifying silicosis into 3 stages was used. In 18 (12·7%) of cases there was a discrepancy of at least one stage between the clinico-radiological and pathological assessments, but in only 13 (9·7%) was this considered as undoubtedly due to faulty radiological classification. In 8 cases the amount of silicosis was overestimated, in 5 underestimated, on the chest X-ray. In 7 cases the assessment of compensation was at fault. The reasons for the disagreement are discussed and numerous illustrative cases are described in great detail.

[This interesting paper would have been even more useful had figures for the amount of dust in the lungs been included.] *I. T. T. Higgins*

MILIJIC, B. & MILETIC, Vida. Su un caso di silicosi a rapida evoluzione. [**On a Case of Rapidly Evolving Silicosis**] *Med. d. Lavoro.* 1959, Nov., v. 50, No. 11, 679–82, 1 fig. [12 refs.]

The English summary appended to the paper is as follows:—

"A case is reported of rapidly evolving silicosis in a 25 year old worker who was employed for 13 months in the digging of a tunnel for the Mavrovo hydro-electric power station, in the People's Republic of Macedonia. The tunnelling was performed in the dry with no protective measures and it produced a great amount of dust. The rapidity of the onset and the further course of the disease can be explained by the massive inhalation of silicotigenic dusts and by a predisposition to the disease. Such predisposition may be due either to a deficient pulmonary autodepuration or to a particular state of immunological hyperreactivity of the subject which was shown in this case by the behaviour of serum proteins. It is concluded that detailed periodical controls with clinical and laboratory investigations of the workers exposed to silicosis hazards may be very useful."

GITTER, A. & SELIG, R. Funktionsdiagnostische Probleme in der Silikose-Begutachtung. I. Mitteilung. Methodik und Ergebnisse spirographischer Messungen der Vitalkapazität und des Atemstosstestes im Vergleich zur spiroergometrischen Leistungsprüfung am Metabolimeter nach Böhlau. [**Problems of Lung Function Assessment in Silicosis. Part I. Vital Capacity and Forced Expiratory Volume compared with an Exercise Test using the Böhlau Metabolism Meter**] *Ztschr. f. ärztl. Fortbildung.* 1959, July 1, v. 53, No. 13, 829–35, 4 figs. [22 refs.]

In this paper the authors describe the spirometer they use to measure ventilatory function and give the mean vital capacity (VC) and the half and one second forced expiratory volume (FEV) percentages in a group of 550 cases of silicosis, approximately half of whom had Stage I and a quarter each Stages II and III. The vital capacity (expressed as a percentage of an expected value) was above the normal lower limit of 80% at all stages of silicosis. Both the 1 and ½ second FEV% were below the normal lower limits and fell with the stage of silicosis, the former from 65·5% in Stage I to 62·5% in Stage III, the latter more steeply from 48·8 to 39·5%.

In a comparison of these ventilatory measurements with the results of an exercise test the recovery quotient fell *pari passu* with the FEV% with increasing stages of silicosis. The VC on the other hand showed no consistent trend with X-ray category. The authors conclude that the vital capacity is an inadequate measure of ventilatory impairment but that the FEV is useful particularly the ½ second test.

[The main interest of this paper is the apparently greater sensitivity in separating the stages of silicosis of the ½ second over the 1 second FEV.] *I. T. T. Higgins*

BUCKUP, H. Überwachungsuntersuchungen Silikosegefährdeter. [**Supervision of Workers in Industries with a Silicosis Risk**] *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1959, Nov. & Dec., v. 9, Nos. 11 & 12, 257–63; 283–7. [13 refs.]

This paper reviews the organization and regulations for silicosis protection in Germany, including the occupations covered in Western Germany and in the Democratic Republic, the qualifications, training and experience of medical officers, and the extent and frequency of the examinations required. *I. T. T. Higgins*

ILIC, S., KARAJOVIC, D., PERISIC, S. & CVETKOVIC-KRISTL, D. L'hypersensibilité cutanée vis-à-vis du cément et des chromates chez les ouvriers de l'industrie du cément. [**Cutaneous Hypersensitivity to Cement and to Chromates in the Cement Industry**] *Acta Med. Iugoslavica.* 1959, v. 13, No. 3, 332–8, 6 graphs. [10 refs.]

The investigation which is shortly described in this paper was undertaken to determine by skin tests the sensitivity of workers in 2 cement factories to both cement and to chromates. About 200 male workers in each of the 2 factories were examined and the results compared since it had been stated that the cement from the factory at Popovac contained chromate but that the cement from the factory at Beočin did not.

Analysis of the cement from the latter showed, however, that it did contain traces of potassium dichromate. Skin tests with a 0·5% solution of potassium dichromate and with 20% and of 40% suspensions of cement demonstrated skin sensitivity in 31 (14·5%) workers at Popovac of whom 7 reacted to both test agents, 16 to chromate and 8 to cement. At Beočin there were 7 positive reactors—1 to both test agents, 1 to cement and 5 to chromate.

These results are shortly analysed. It appears that skin hypersensitivity is not common among cement workers but tends to be more frequent in the older age-groups; in those with long periods of work with cement and in certain stages of the manufacture in which workers sweat heavily. Chromate sensitivity was more frequently found than cement sensitivity. In general the sensitivity was latent for only 3 cases of eczema were found among all the workers in the 2 factories.

M. E. Delafield

KARAJOVIC, D., DANILOVIC, V., VERBIC, N., ĐORDEVIC, V., POPOVIC, D., MILOSAVLJEVIC, Ž., ĐORDEVIC, S., SLAKOVIC, V., SAVIC, D. & MALESVIC, L. Erforschung der Allergie bei Arbeitern in der Zementindustrie. [**Allergy in Workers in the Cement Industry**] *Acta Med. Iugoslavica.* 1959, v. 13, No. 3, 339–45.

In this paper there is an account of the clinical findings in the examination of the workers at the 2 cement works at Popovac and Beočin whose reactions to skin sensitivity tests were described in the previous paper. Among 425 workers were found 57 cases of chronic bronchitis, 21 of chronic bronchitis with emphysema, 6 of bronchial asthma and 7 cases of bronchitis of asthmatic type. The cases with asthma were considered to be allergic manifestations. These clinical findings and also the results of full examination of ear, nose and throat of about 100 workers are discussed in relation to the results of the skin tests. The high incidence of non-allergic and allergic illnesses is considered to be caused in part by the heavy physical work which is needed in the absence of sufficient mechanization, inadequate ventilation and the neglect of measures for the personal protection of the workers. Further research is needed to determine the constituents of the cement dust which are sensitizing.

M. E. Delafield

AMERICAN INDUST. HYG. ASS. J. 1959, Oct., v. 20, No. 5, 341–73, 11 figs. [Numerous refs.] **The Toxicological Basis of Threshold Limit Values.**

This series of papers consists of reviews, analyses and mathematical formulae, the 3rd and 5th including experiments.

1. *Experience with Threshold Limit Values Based on Animal Data.* H. F. SMYTH, Jr., 341–45.

The author examined the history of the TLV of 148 substances, listed in 1953 or earlier, to determine which criteria had given and therefore presumably would in future give, stable values. 87 original values were not changed. Of 45 based on repeated inhalation or feeding experiments, only 15 were changed, none since 1947 and all except 1 reduced. This method appeared as sound as any, especially when a safety factor had been applied. No other guide for improving designs of toxicological studies was found.

2. *Pathological and Biochemical Criteria.* V. K. ROWE, M. A. WOLF, C. S. WEIL and H. F. SMYTH, Jr., 346–49.

Results of 22–25 years' toxicity studies involving repeated administration were analysed. Tables of 3 kinds of investigation show frequencies of positive results in relation to the lowest dose producing any effect. Except when specific investigations were indicated, *e.g.* for expected cholinesterase depression, combination of 5 investigations—on growth and liver and kidney weights and pathology—gave most information. If limited to these 5, the lowest dose to cause any effect would have been discovered in 96% of some hundreds of studies.

3. *Physiological Criteria.* J. A. ZAPP, Jr., 350–56.

Impaired judgment or delayed reaction tell much where organic lesions may not be detected. Non-destructive physiological tests in assessing the environment or in animal experiments may help men to use chemicals without suffering even minimal body injury—an intermediate state between health and illness accompanied by tension, strain or discomfort. Precedents are found in the work of Claud Bernard, Pavlov and Selye. Experiments with non-toxic levels of chlorotrifluoroethylene demonstrate alterations in blood pressure and blood counts in dogs and in renal function in rats, and this last is also shown by $HgCl_2$ in doses below LD50. Russian data show lower TLV when based on muscle output or conditioned reflexes than on symptoms and morphological changes.

4. *Theoretical Approach to Prediction of Toxicity of Mixtures.* W. L. BALL, 357–63.

This necessary approach is based firstly on possible physical and chemical reactions outside and inside the body, secondly on the principles of Selye's theories of combined stressors to judge physiological actions and finally on mathematical treatments of dosage-response curves as used by entomologists to predict effectiveness of insecticide mixtures. Formulae are given for 3 types: similar joint action, likely with chemicals of related constitution; independent action where chemicals act at different sites; and synergistic or antagonistic action.

5. *The Experimental Inhalation of Vapor Mixtures by Rats, with Notes upon the Relationship between Single Dose Inhalation and Single Dose Oral Data.* U. C. POZZANI, C. S. WEIL and C. P. CARPENTER, 364–69.

To determine the relationship between the inhalation LC50 of composite vapours and the LD50 of individual components, 15 commercial chemical mixtures and 3 chemical pairs were tested. The highest correlations were found between the predicted inhalation and observed inhalation values. Lower correlations between observed oral and observed inhalation values suggest that it is possible to estimate with fair reliability a single dose LC50 value from oral data. Though the formula to predict the LC50 and LD50 values of mixtures is theoretically suitable only when there is similar joint action, it is fairly accurate for predicting

the single dose toxicity of mixtures from the single dose toxicity data of the components.

6. *Report of Prague Symposium on International Threshold Limit Values.* W. L. Ball, 370–73.

The International Symposium on Maximum Allowable Concentrations of Toxic Substances in Industry was held by the Permanent Committee and International Association on Occupational Health and the International Union for Pure and Applied Chemistry. 4 sections considered definitions, methods, biological testing and atmospheric analysis. The recommendations are transcribed. In brief, collection and publication of information and choice of methods were asked of the 2 convenors, and continuously revised international MAC tables of the Permanent International Commission of Industrial Medicine. The MAC should be that value which leads to no aberrations, excepting hypersensitivity, judged by the most sensitive indices for continuous working, based on scientific evidence and weighing other environmental factors and possible cumulative effects. *M. Patricia Fitzsimons*

McCaldin, R. O. & Hendrickson, E. R. **Use of a Gas Chamber for testing Air Samplers.** *Amer. Indust. Hyg. Ass. J.* 1959, Dec., v. 20, No. 6, 509–13, 3 figs.

Moreo, L. Su una sorgente poco nota di saturnismo: la fabbricazione di virole per lampadine elettriche. [**A Little-Known Source of Lead Poisoning; the Manufacture of Ferrules for Electric Light Bulbs**] *Med. d. Lavoro.* 1959, Nov., v. 50, No. 11, 673–8, 1 fig. English summary.

The author reports 2 cases of Pb poisoning 1 female and the other male in operatives making the ferrules for electric bulbs. The poisoning is considered to have arisen through the use of a "vitrite" a soft glass (into which the 2 metal supporters for the filament are placed) with a Pb content which varied from 0·035% to 6%.

The female patient had worked for 11 years a machine which automatically placed a blob of the fused glass on to the top of the ferrule, but she had had attacks of colic, vomiting, and oliguria 3 months before admission. She then had a blue line, enlarged liver, signs of kidney damage, and a free erythrocytic protoporphyrin of 340 μgm.% and a post-versenate urinary Pb of 8,250 μgm./24 hours. The man had worked at one of the furnaces removing the fused glass for 29 years and 24 months before admission had had an obvious attack of Pb poisoning.

No estimation of the Pb content of the air near the furnaces was carried out but a laboratory experiment showed that it was possible for as much as 3–4 mgm.Pb/cu.m./hour to be emitted.

The author is certain that these 2 cases arose from their work but points out that they are the first to be recorded in the literature. The operatives may have been working with a glass with a high Pb content and the aspiration apparatus was not functioning.

W. K. Dunscombe

Saita, G. Il dosaggio della protoporfirinemia e dell'eliminazione del piombo dopo versenato di calcio nella diagnosi di saturnismo pregresso. [**The Determination of Protoporphyrinaemia and Lead Elimination after Calcium Versenate in the Diagnosis of former Lead Poisoning**] *Med. d. Lavoro.* 1959, Nov., v. 50, No. 11, 659–72. [20 refs.] English summary.

The author states that an increase in the free erythrocytic protoporphyrin (PPE) is one of the cardinal signs of lead poisoning; it is often found before the appearance of stippled cells or increased urinary coproporphyrin while it persists even after the other usual tests have returned to normal limits and is only slightly altered by Ca-EDTA treatment.

This increased PPE is due to the biotoxic blocking action of lead on the synthesis of haem especially at the stage when iron is incorporated into the protoporphyrin.

He therefore estimated the PPE level especially as regards the limits of time within which it could be of value for retrospective diagnosis of lead poisoning, and at the same time the usefulness of determining the urinary lead after intravenous injection of 1 gm. calcium versenate every 12 hours for 2 days (PbPV) was tested. The investigations were carried out at the Milan clinic on patients sent by the National Industrial Accident Insurance Board (INAIL) in whom the usual laboratory tests indicative of lead poisoning had given normal values. Some of the patients had given up the job where they had been exposed to risk for a number of years. Normal levels were taken for PPE as not more than 100 μgm. per 100 cc. and for urinary PbPV not more than 1,000 μgm./24 hours.

The patients formed 4 groups as follows: (A) 12 with both increased PPE and PbPV; (B) 12 with normal PPE and increased PbPV; (C) 2 with increased PPE and normal PbPV; (D) 7 both tests with normal values.

Of the patients in group A those with the most florid symptoms usually showed the highest levels though 1 patient who had not had contact with lead for 8 years and complained of colic, still had a PPE of 141 μgm.% and PbPV of 1,600 μgm./24 hours. Some of the PbPV levels were also very high in group B. 1 smelter who had not had contact with lead for 9 years still had a PbPV of 2,200 μgm./24 hours but both he and another patient with renal arteriosclerosis and hypertension who had no contact for 11 years were accepted for compensation. The 2 patients in group C showed so slight an increase that they can hardly be taken as anomalous results; both had some pathological liver condition.

Saita states that the PPE estimation should be performed in all suspect cases and considers that a significantly increased PPE can be met with up to 8 years after Pb exposure has ceased. No case regarded as Pb poisoning had an increased PPE without an increased PbPV also. The importance of these findings from the point of view of industrial insurance is emphasized.

[This paper should be read in full but clinicians will be interested to note that 2 patients complaining of abdominal pains who also had hypertension were accepted for compensation on the basis of these 2 tests

though contact in 1 case had ceased for 7 and in the other for 8 years.] *W. K. Dunscombe*

FRIED, Joan F., SCHUBERT, J. & LINDENBAUM, A. **Action of Edathamil (EDTA) Analogs on Experimental Lead Poisoning.** *Arch. Indust. Health.* Chicago. 1959, Dec., v. 20, No. 6, 473–6. [22 refs.]

"Three chelating agents, ethylenediaminetetra acetic acid (edathamil), diethylenetriaminepenta acetic acid (DTPA), and 2:2′-bis(dicarboxymethyl) amino diethyl ether (BAETA), have been compared for their protective action against acute lead poisoning in rats. The lead chelates of edathamil and DTPA were much less toxic than lead nitrate. Both calcium edathamil and CaDTPA were ineffective when given one hour after the injection of lead nitrate. BAETA was ineffective in both cases. The explanation for these results is discussed in terms of the relative affinities of these three chelating agents for Pb ++ and Ca ++ and of Pb ++ for the tissue proteins."

FALEG, G. & LENZI, R. Le alterazioni della laringe nell'intossicazione cronica professionale da mercurio. [**Affections of the Larynx in Chronic Occupational Mercury Poisoning**] *Rass. Med. Indust.* Rome. 1959, July–Aug., v. 28, No. 4, 299–305. [20 refs.] English summary (8 lines).

The authors describe investigations carried out on 105 male and 195 female workers in the felt hat and fur industries who were suffering from chronic mercury poisoning and who all were receiving compensation at rates varying from 21 to 100%. None had worked at their trade for less than 15 years. Among them 22 men, and 52 women had some laryngeal condition.

This was classified into (a) allergic; (b) nervous; (c) catarrhal. (a) The allergic condition was seen in 5 men and 10 women. The vocal cords were mainly affected though the functional disturbance was greater than the laryngoscopic appearances might lead one to think; attempts to start work with Hg caused exacerbation.

(b) The nervous condition was seen in 4 men and 14 women. Aphonia was the main symptom; sometimes there was either partial or complete paralysis of the muscles of phonation seen mainly in women; it was particularly noticeable in patients in whom the chronic Hg poisoning was manifested by predominantly neuropsychological symptoms.

(c) The catarrhal condition occurred in 13 men and 28 women. The clinical picture was that of a chronic catarrhal laryngitis with dysphonia. Examination showed mucosal hyperaemia, hyperadduction of the ventricular bands in phonation and particularly chronic laryngitis of the vestibule. This was seen mainly in women but especially in those working at jobs where the Hg vapour could be inhaled.

The authors summarize by saying that 24·66% of their patients had a condition referable to the larynx and that this organ can frequently be injured in Hg poisoning; chronic catarrhal laryngitis is the most frequent form of damage. *W. K. Dunscombe*

SWENSSON, A., LUNDGREN, K. D. & LINDSTRÖM, O. **Retention of Various Mercury Compounds after Subacute Administration.** *Arch. Indust. Health.* Chicago. 1959, Dec., v. 20, No. 6, 467–72. [10 refs.]

"Groups of rats were given different mercury compounds in the drinking water in amounts corresponding to 2 mg. per liter of water for periods up to three weeks. The compounds studied were mercuric chloride, mercuric nitrate, phenyl mercuric acetate, methyl mercuric hydroxide, and cyano (methyl mercuri) guanidine.

"The compounds were labeled with the isotope Hg^{203}, and the determinations of the mercury content of different organs were made with scintillation technique.

"Both types of organic compounds gave much higher mercury concentrations in the blood than did the inorganic compounds.

"The inorganic compounds accumulated in the plasma of the blood; the organic compounds were bound mainly to the red blood corpuscles.

"The organic compounds gave much higher mercury concentrations in the organs studied, brain, liver, and kidney.

"The inorganic compounds gave a very low mercury content in the brain. The organic compounds gave higher mercury values in the brain.

"The ratio between the blood and brain mercury contents seems to be constant for each substance and indicates a distribution equilibrium."

MINDEN, H., BRÜCKNER, C. & SIMON, J. Beitrag zur Cadmiumvergiftung. Symptomatik und experimentelle Untersuchungen. [**Cadmium Poisoning; Symptomatology and Experimental Investigation**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 5, 531–46, 8 figs. [13 refs.]

Cadmium in its occurrence, and physical and chemical characteristics, shows similarities to zinc and mercury, but differs from zinc in that its acute effects are unaccompanied by fever; it resembles mercury in causing renal injury though the authors do not consider that this plays an essential role in the symptom complex. It is stored chiefly in the liver and the kidney cortex and is excreted chiefly by the kidney.

An outstanding feature of cadmium poisoning is the latent period of 24 to 36 hours between the initial non-specific, and the later severe specific symptoms. The initial symptoms—headache, gastro-intestinal disturbance, lassitude, irritability, palpitation, constriction of the chest, shortness of breath, giddiness, cold or heaviness of the extremities and lowering of blood pressure—have been attributed to adrenal cortex deficiency—a non-specific stress reaction—the later symptoms to inhibition of certain enzymes, especially the sulphydryl group.

In acute fatal poisoning a non-febrile pneumonia, and fatty degeneration of the liver and kidney, have been reported; in chronic poisoning nasal irritation, a yellow ring round the teeth, loss of smell, proteinuria, anaemia, loss of weight, increased sedimentation rate, emphysema and digestive disturbance. The urinary protein has a molecular weight of 20,000 to 30,000.

The authors have examined the effects of subacute poisoning in rabbits subjected to repeated intravenous injection of a 0·3% solution of cadmium sulphate with regard to the blood sedimentation rate, the serum albumin fractions, the lipoproteins, the blood picture and kidney function. The total amount of cadmium as metal in the blood after a total dose of 375 to 471 mgm. of cadmium sulphate was between 200 and 280 μgm.%

The blood sedimentation rate showed a marked rise. Electrophoretic examination of the serum showed, during the first day, a fall in the total albumin, and alpha and beta globulin, but a very slight, not significant, rise in gamma globulin which tended to subside later.

A comparison of these variations with those occurring in lead poisoning showed that in the latter there was a slight decrease in total albumin, with a simultaneous increase of all 3 globulin fractions; this is said to indicate that the cadmium effect is a specific one. The lipoproteins showed an increase corresponding with that of the alpha and beta globulins.

The blood picture showed a fall in haemoglobin with a slower fall in erythrocytes, and consequently a low colour index; no change was noted in the total white cell or differential count except a moderate eosinophilia (up to 4%). The body weight remained constant when that of the control animals was still rising. There was no porphyrinuria, and no osteoporosis, as postulated by several French authorities.

All the animals excreted small amounts of albumin in the urine but there was no increase in residual nitrogen.

It is concluded that the variations in the serum albumin fractions is not due to disturbance of synthesis of albumin but to a marked increase of the lipoprotein fraction which is also the cause of the increased sedimentation rate. *Ethel Browning*

Bozovic, B., Savicevic, M., Milijic, B., Jocic, V., Kenda-Jelicic, D. & Petrovic, L. **Allergic Disease in the Antimony Mine.** *Acta Med. Iugoslavica.* 1959, v. 13, No. 3, 374–7.

This is a short paper in which there is a description, without much detail, of the results of an investigation of the health of 135 workers, mostly between 20 and 50 years of age, in an antimony mine. The air of the mine has a high temperature, contains increased concentrations of SO_2 and CO and is of "abundant dustiness". The dust contains SiO_2, Sb_2O_5, As_2O_3 and PbO.

The most important of the illnesses suffered by the workers were "Acute inflammations of the upper respiratory tract" which represented 29% of the total, but "allergic diseases of the respiratory tract were not found at all". Skin tests carried out in 118 workers none of whom had any history of allergic manifestations showed that a high proportion of the men gave a positive result, *i.e.* "sensitive to general dust (28), bacteria (23), wheat parasites (21), mould (14), bedclothes (6) and to the allergen of dust from the working place (5 workers)". *M. E. Delafield*

Lewis, C. E. **The Biological Actions of Vanadium. III. The Effect of Vanadium on the Excretion of 5-Hydroxyindolacetic Acid and Amino Acids and the Electrocardiogram of the Dog.** *Arch. Indust. Health.* Chicago. 1959, Dec., v. 20, No. 6, 455–66, 6 figs. [32 refs.]

Metabolite excretion studies form part of this discussion and review of the literature. There is a possibility that vanadium may be a cofactor of monoamine oxidase which, among other actions, converts serotonin, 5-hydroxytryptamine (5-HTA) to its major metabolite—5-hydroxyindolacetic acid (5-HIAA). Symptoms caused by increased circulating serotonin are based upon smooth muscle contraction, and many symptoms of acute vanadium intoxication are similar [see this *Bulletin*, 1959, v. 34, 1139]. To evaluate the possibility, urinary excretion of 5-HIAA was investigated in dogs before and after intravenous injection of a 2% solution of sodium metavanadate, 2·5–5 mgm. per kgm. Adequate urine volume was secured by saline infusions. The cause of the decreased excretion, which lasted for at least 4 hours, was probably twofold: alterations in blood concentrations and of renal tubular function. Conclusions from similar experiments after preliminary injection of 5-HTA were speculative. There was less evidence to suggest that high vanadium doses decreased the conversion of injected 5-HTA to 5-HIAA or that smaller doses increased it. However, the results were consistent with the possibility that the lower dosage was closer to the optimum concentration of cofactor if the possibility stated at the beginning were true and if 5-HIAA excretion reflects monoamine oxidase activity.

Transient albuminuria and bilirubinuria probably represented kidney and liver injury. Increased excretion of keto acids was of interest in view of the possible consequences of interference with acetate utilization in cholesterol synthesis (*ibid.*, 910). The urine contained no sugar or acetone. Amino acid chromatography studies showed excretion of certain amino acids not normally present in dog urine.

Illustrated electrocardiograms are sufficiently stable to permit analysis of serial results, difficulties from positioning and heart rate having been resolved. Increased amplitude of the T-waves was followed by an alteration in the ST-segment, which persisted for 6–10 hours, disappeared within 24 hours and left no sequelae. *M. Patricia Fitzsimons*

Gilbert, G. J. & Glaser, G. H. **Neurologic Manifestations of Chronic Carbon Monoxide Poisoning.** *New England J. of Med.* 1959, Dec. 10, v. 261, No. 24, 1217–20, 2 figs.

A case report from the Section of Neurology at Yale University illustrates the symptomatology and diagnostic difficulties of this insidious and controversial disease. It is believed that chronic CO poisoning is characterized by persistent symptoms and signs—particularly those of an organic confusional state—between exposures and exacerbated by them, and correlated with high, fluctuating, slowly declining blood levels of CO.

A policeman aged 50 was found during his second admission to hospital to have been exposed to 2 common sources of CO, duty in heavy traffic and in a badly ventilated garage where police-car radios were often charged by petrol-driven motors. Afterwards a third source was a petrol-powered farm tractor with the exhaust at head level. During the first admission the diagnosis was psychomotor seizures and cerebral atrophy, possibly related to an old head injury. Treatment with anticonvulsant drugs which he had had for 2 years was continued. He returned to work improved in health but was re-admitted some 6 months later. The occupational history was investigated. Chronic CO poisoning was verified by finding the blood to be 20% saturated with CO 30 hours after ceasing work. Treatment was stopped. He remained essentially asymptomatic except during the tractor episode.

The symptoms, which had begun 4 years previously during traffic duty, were anorexia, weight loss, a fluctuating organic mental syndrome and recurrent episodes of unconsciousness, each attack preceded by dizziness and ataxia, usually in the afternoon. Investigations, fully reported, were mainly negative. Hyperthyroidism, suggested by sweating and fine tremor, was excluded by metabolic tests, the blood iodine being in the hypothyroid range and the radioactive iodine uptake normal. There was transient albuminuria. The serum glutamic oxalacetic transaminase was slightly elevated. Serial electroencephalograms after withdrawal from exposure showed progressive clearing of focal and paroxysmal abnormalities, correlated with clinical improvement.

M. Patricia Fitzsimons

WEIST, H. J. Schwefelkohlenstoffbestimmungen im Blut ohne und bei Schwefelkohlenstoff-Exposition. Das Verhlaten des Blut- und Harntiters von Chemiefacharbeitern der Kunstfaser- sowie Viscoseindustrie. [**Estimation of CS_2 in Blood, with and without Exposure. Relation of Blood and Urine Levels in Chemical Workers in Synthetic Fabrics and Viscose Industry**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 4, 430–41, 5 figs. [16 refs.]

By means of a colorimetric method (titrating with N/1,000 iodine solution) estimations were made of the CS_2 blood levels in 10 persons with no or very slight exposure, of 19 chemical workers in a factory producing CS_2, and of 24 in a viscose process.

The author's values for "normal" persons differ considerably from those of 2 other investigations; he found none, in contrast to the 200 μgm. per 10 cc. postulated by RODENACKER in 1953, and 0 to 15·2 μgm. by SCHRAMM and HENRICH in 1942 (*Reichsarbeitsbl.*, v. 3, 145). There is a similar discrepancy between the values for moderate and severe exposure.

In the chemical factory, where the atmospheric concentrations of CS_2 varied from traces to 50 mgm. per cubic metre, the average blood level was 30·74 μgm. per 10 cc., highest (80 μgm.) in one man who had worked in especially unfavourable conditions. The most significant point arising from this investigation was the fact that before the shift began the blood CS_2 level was nil, and at the end had risen to levels between 6·07 and 80 μgm. One of these men, after 4 hours in the fresh air, showed complete absence of CS_2 in the blood, and another, who had had 4½ hours away from his former work but not entirely away from the factory, showed only a fall from 11·91 to 5·95 μgm.

The urinary CS_2 was in 15 cases out of 18 lower than the blood, in 3 cases higher (average 15·6 μgm.).

In the viscose factory, where the air concentration was between 50 and 60 mgm. per cubic metre the blood level was significantly higher than in chemical production, and varied in different departments, the highest being in the cutting section—an average of 92·6 μgm., and in general again higher than in the urine. In contrast to the chemical workers, the viscose workers never showed complete absence of CS_2 in the blood even before the shift, and in one case the level was higher at the beginning than at the end.

Thus, with greater exposure, the CS_2 is retained in the blood and may accumulate, so that at some time the limiting value may be exceeded and symptoms of chronic poisoning occur. None of these persons showed definite symptoms of ill-health, but in 3 with indications of incipient poisoning the blood level was not significantly higher than the rest. It was therefore considered that, within the scope of this investigation, estimations of CS_2 in the blood could not be regarded alone as a diagnostic measure of chronic CS_2 poisoning.

Ethel Browning

JOHNSTONE, R. T. **Death due to Dioxane?** *Arch. Indust. Health.* Chicago. 1959, Dec., v. 20, No. 6, 445–7.

A medical file, all that the author had to go upon and admittedly lacking in certain evidence, nevertheless contained features which warrant publication as the "first of its kind case" and which suggest that exposure to dioxane for 1 week caused the 21-year-old patient's fatal illness. He was admitted to hospital with epigastric pain radiating to the lumbar regions, lumbar muscle spasm and high blood pressure. Though a heavy beer drinker he was not intoxicated. Some hours later occipital headache was followed by a convulsion and cyanosis, shock and unconsciousness. Improvement followed treatment, and anuria for 5 days was partially overcome, the non-protein nitrogen only rising 5 mgm.%. Deterioration was observed next day accompanied by agitation, was followed by coma, papilloedema, absence of reflexes and death. The liver showed centrilobular necrosis, the kidneys focal necrosis and moderate nephrosclerotic changes, the brain focal malacia secondary to anoxia and oedema; there was bronchopneumonia.

The patient had used liquid dioxane, from a bucket held between his knees, to free his hands and the workbench from glue which dropped from aluminium sheeting overhead. There was no exhaust ventilation. Atmospheric concentrations of dioxane ranged from 208 p.p.m. to 650, average 470. The MAC is 100 p.p.m. Dioxane, 1,4-diethylene, has caused liver and kidney damage in animals after inhalation and skin penetration. The syndrome was similar to that of 5 fatal English cases where exposure after 16 months had been intensified (*Guys Hosp. Rep.*, 1934, v. 84, 267). The

alcoholic may be more susceptible. No other cause of death was apparent.

It seemed fair to conclude that: no pathological disturbances have been reported in man from daily exposure to permissible concentrations; exposure to high concentrations can result in acute illness and possibly death; and the brain as well as the liver and kidneys may be involved. *M. Patricia Fitzsimons*

DOUILLET, M., BOURRET, J. & CONVERT, A. Les aminotumeurs professionnelles des voies urinaires provoquées par la benzidine. [**Occupational Tumours of the Urinary Tract caused by Benzidine**] *Arch. Malad. Professionnelles.* Paris. 1959, Nov.–Dec., v. 20, No. 6, 713–33, 4 figs.

Medical supervision of the workers in a benzidine manufacturing plant began in 1942. Case-notes of 13 workers treated for growths of the bladder and ureter are illustrated by urograms, and some extend over 16 years. A discussion of symptomatology and development, diagnostic measures, indications for and methods of treatment and results follows a general account of the history, aetiology, statistics, toxicology and pathology of the occupational disease caused by alpha- and beta-naphthylamine and benzidine.

Exposure to benzidine was sometimes discontinuous and lasted for periods of 2 to 21 years. The latent period before bladder tumours developed ranged between 10 and 26 years, mean 16, and, before 5 men developed ureteral tumours, was 15–23, mean 19. For very malignant tumours it was about 12, maximum 17. There were 5 carcinomata. The youngest patient was 43, the oldest 62, mean age 54. 5 died and the condition of the only survivor of the ureteral disease in 1958 was precarious.

In prevention, many important technical, environmental and medical measures are argued—from manufacture ceasing at the sulphate stage in paste form to supervision of cleaning after work-hours when the plant is cool; from employment only of older workers to medical rejection of men with susceptible histories or certain diseases. Annual cystoscopy, the disadvantages and difficulties of which are recognized, was preferred to exfoliative cytology because of the small population.

Medico-legal problems lead to the suggestions that occupational bladder disease should be re-defined as "lesions of the urinary tract . . .", and that the period within which compensation may be claimed after ceasing scheduled work should be lengthened from 15 years to 20 or 25, in order to allow for ureteral growths and also for low and short exposures when the latent period may be prolonged. *M. Patricia Fitzsimons*

WETHERHOLD, J. M., LINCH, A. L. & CHARSHA, R. C. **Hemoglobin Analysis for Aromatic Nitro and Amino Compound Exposure Control.** *Amer. Indust. Hyg. Ass. J.* 1959, Oct., v. 20, No. 5, 396–405, 10 figs.

Abnormalities in haemoglobin analyses preceded by 24 hours the appearance of cyanosis and methaemoglobinaemia. Control measures which had been satisfactory for toluidines, phenetidines, alpha-naphthylamine, nitrotoluidines and anisidines were not effective enough when chloroaniline production began. Annual haemoglobin average values from 1943 to 1957 show a correlation with the number of cases of cyanosis in several processes. Other charts show the relationship of an incidence of 30% of abnormal blood specimens to incidence of cyanosis and exposure evaluation. A blood specimen was considered abnormal if: methaemoglobin exceeded 10%; the difference between the acid haematin and the oxidized haemoglobin values for haemoglobin exceeded 10%; haemoglobin fell below 13 gm. per 100 ml. blood. Patients with abnormalities were watched and the analyses repeated at short intervals.

For acute exposure control, every day about 4 from each group working in areas of potentially severe exposure were examined and if the end of the day percentage of abnormal haemoglobin analyses reached 30%, action was taken. For chronic exposure control, routine analyses were made quarterly, and also whenever patients attended the medical department for injury or illness. Results were also scrutinized weekly and monthly to find whether abnormal trends reached 30%. The application of results to the solution of exposure problems, often at sub-cyanosis levels, could take the form of pin-pointing unsatisfactory equipment or working methods or detecting susceptible workers. The study also demonstrated differences between chloroanilines and toluidines in cyanosis potential. Practical control procedures and protective measures are discussed and examples given. Air analyses and blood analyses did not correlate sufficiently to be of use because these fat soluble aromatic compounds are absorbed mostly by skin contact or from steam-borne mists.

Recent steadily declining trends in cyanosis and abnormal haemoglobin results show that control measures were effective, and suggest that the permissible abnormal specimen limit could be reduced to 20%.

M. Patricia Fitzsimons

GOLDSTEIN, I. & POPOVICI, C. L'action du 2, 3 Dimercaptopropanol (BAL) dans l'intoxication experimentale au nitrobenzene. [**The Action of 2, 3 dimercaptopropanol (BAL) in Experimental Nitrobenzene Intoxication**] *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1958, v. 2, No. 2, 237–43. [20 refs.]

Treatment with 2, 3 dimercaptopropanol is considered to exert a protective effect in nitrobenzene poisoning by bringing about a reduction in the concentration of methaemoglobin in the blood, and the authors have investigated this point in animal experiments. Of 30 rats treated with nitrobenzene in a single dose of 0·64 gm. per kgm. body weight 14 died, whereas in groups of rats treated similarly with nitrobenzene and given 2, 3 dimercaptopropanol in doses of 10, 20 and 30 mgm. per kgm. respectively the mortality was increased and 26, 27 and 26 died. 4 hours after intoxication with nitrobenzene the proportion of methaemoglobin to haemoglobin was 30% and rose to 50% after 12 hours, whereas in rats treated with 2, 3 dimercaptopropanol

after intoxication the proportion was only 19% at this time, although there was more sulphaemoglobin present. A similar fall in methaemoglobin and rise in sulphaemoglobin was also seen in 6 dogs given nitrobenzene and treated with 2, 3 mercaptopropanol. *D. J. Bauer*

AMDUR, M. L. **Accidental Group Exposure to Acetonitrile—a Clinical Study.** *J. Occup. Med.* Chicago. 1959, Dec., v. 1, No. 12, 627–33, 2 figs.

Investigation and study of the clinical course in 9 men whose illness was delayed after working under hastily improvised and unsafe conditions with this organic cyanide illustrate several aspects of industrial medicine. Toxic manifestations in the 8 survivors seemed to be the result, not of the primary toxicity of acetonitrile, methyl cyanide, but of the detoxification mechanism, *i.e.* the overproduction of thiocyanate into which cyanide is converted by rhodanese. [See this *Bulletin*, 1959, v. 34, 1142.]

The patients were found, 1 already semiconscious and grey with bradycardia, hypotension and paresis, when news of the fatal case, received shortly after the supervisor had complained of sickness, initiated investigations. The man who died had awakened 4 hours after leaving work, with chest pain, nausea, vomiting and convulsions, and was spitting blood; he died 10 hours later. Onset and degree of illness varied with blood cyanide and serum thiocyanate concentrations. When the latter is below 12 mgm.% symptoms may include weakness, fatigue, exhaustion, somnolence, apprehension, nausea, diarrhoea, abdominal pain, skin eruptions and possibly thyroid dysfunction; above this they include angina, mucous membrane bleeding, motor irritability, confusion, delirium, convulsions, paralysis and coma. Nearly all the patients had symptoms of thiocyanate intoxication. Blood cyanide was slow to fall in 1, conversion being impeded by hyperthyroidism. In the fatal case the tissue cyanide content was high except that of the liver, which was zero, probably reflecting the high liver rhodanese [thiosulphate transsulphurase] content.

The patients were men who had encountered technical difficulties in a second attempt to line a chemical tank with corrosion-resistant materials. To overcome viscosity they heated the primer and mixed it with the acetonitrile materials, and to overcome rapid setting they eliminated the positive ventilation. 6 men working nearby had no symptoms, their blood cyanide was zero and serum thiocyanate below 3 mgm.%.

The work was accomplished, with the correct method and adequate ventilation. Air sampling showed no free HCN and not more than 17 p.p.m. of organic cyanide. *M. Patricia Fitzsimons*

POZZANI, U. C., CARPENTER, C. P., PALM, P. E., WEIL, C. S. & NAIR, J. H. **An Investigation of the Mammalian Toxicity of Acetonitrile.** *J. Occup. Med.* Chicago. 1959, Dec., v. 1, No. 12, 634–42. [18 refs.]

Different animal species varied in toxic response to acetonitrile, and human volunteers varied in their symptoms. Acetonitrile, methyl cyanide, CH_3CN, is a volatile solvent used in the synthesis of many organic compounds and in oil extraction.

Intraperitoneal injection was more toxic in rats than intravenous injection, possibly because rapid penetration into the liver overwhelmed enzymes. This possibility is supported by differing toxicity after injections in the portal vein or into the tail vein, LD50 being 0·71 and 1·68 ml. per kgm. respectively. In several species inhalation caused death from pulmonary haemorrhage or congestion; some deaths were delayed. Repeated inhalation, in various concentrations, resulted in: lung, liver and kidney changes in rats; cerebral haemorrhage and lung and kidney changes in monkeys; emphysema in dogs; cyanide in blood in dogs and monkeys; and thiocyanate in the urine of all 3 species, and in rabbits after skin-penetration tests.

To determine the ratio between absorbed acetonitrile and excreted metabolite, *i.e.* thiocyanate, monkeys were injected intravenously with acetonitrile and, when depleted, with sodium thiocyanate. More than 12% acetonitrile was converted. The sodium thiocyanate was not entirely excreted. Cyanide formation contributed to death in dogs exposed to high concentrations of acetonitrile. The rapidity with which rats died after large doses by various routes was attributed to the direct action of the intact molecule. At lower concentrations, with delayed deaths, cyanide and other metabolites contributed their effects.

In the volunteers no blood cyanide was found after 4 hours' inhalation of 40, 80 and 160 p.p.m., and no correlation between thiocyanate excretion and acetonitrile concentration: these tests could be unreliable in brief, low exposures. A table shows that acetonitrile is much less toxic than acrylonitrile, for which the maximum permissible concentration, proposed in 1942, is still 20 p.p.m. [this *Bulletin*, 1943 v. 18, 564]. For acetonitrile, an initial standard of not more than 40 p.p.m. is proposed. *M. Patricia Fitzsimons*

DILL, D. B. & JACOBSON, K. H. **Toxicity of Propellant Fuels and Oxidizers.** *U.S. Armed Forces Med. J.* 1960, Feb., v. 11, No. 2, 125–31. [19 refs.]

The foresight of medical officers of the 3 United States Armed Forces resulted in study of health hazards from propellant fuels, fire-extinguishers, hydraulic fluids and other militarily used chemicals, being undertaken in the laboratories at the Army Chemical Centre, Maryland, where there were facilities for comprehensive research. This lecture to the Aerospace Medical Association touches on inter-service planning conferences, numerous chemicals, publications and safety manuals, and summarizes certain toxic effects.

Fatty degeneration of the liver, focal interstitial nephritis and terminal convulsions are caused by hydrazine [this *Bulletin*, 1954, v. 29, 838; 1955, v. 30, 328]; methylation reduces the metabolic effects though it accentuates the nervous stimulation, which can, however, be controlled partially by barbiturates. Chronic poisoning by 1,1-dimethylhydrazine (UDMH) results in anaemia.

High-thrust boron-based fuels for rockets and air-breathing engines are represented by HEF-2 and by

another group, HEF-3 and HiCal-3. They, like penta- and decarborane, affect the central nervous and cardiovascular systems and metabolic pathways. Large doses stimulate and small doses depress the nervous system. Blood pressure first rises and then falls low. Hyperglycaemia sometimes develops. Isolated heart perfusion with HEF-3 caused increase of rate and force. HEF-3 intravenously or intraperitoneally caused pulmonary oedema or haemorrhage. LD50 values show HEF-3 and HiCal-3 with 1 exception to be more toxic than HEF-2.

Some threshold limit values are given: hydrazine 1 p.p.m., UDMH 0·5; the irritant propellant oxidizers—chlorine trifluoride, fluorine and ozone 0·1, NO_2 and N_2O_4 5, nitric acid 10; speculative values for boranes 0·05 or less. These values, set for normal working periods, may be hazardous under military service conditions, especially on board ship or in submarines, and in bioastronautics where exposure may last all day and night. End products of combustion may be toxic to man, animals or plants near launching grounds, *e.g.* boron oxide, relatively non-toxic to mammals, is toxic to plants. *M. Patricia Fitzsimons*

Fabre, R., Chary, R., Bocquet, P. & Jayot, R. État actuel de la toxicologie des hydrures de bore. [**The Present Position of Boron Hydride Toxicology**] *Arch. Malad. Professionnelles.* Paris. 1959, Nov.–Dec., v. 20, No. 6, 701–12. [23 refs.]

High-energy boron fuels for rocket propulsion and aviation have many other uses in the chemical industry, and this account and review of the literature, mainly from American sources, includes the strict precautions necessary in working with these highly toxic boranes. The qualities which make them better in performance than hydrocarbons and other fuel improvers are based on energy unit per mass and volume, ease of storage and even cost. Organic and metallic boranes are touched upon. Diborane, pentaborane and decaborane are described. They are central nervous system and hepato-renal poisons—diborane a pulmonary irritant—and may be absorbed through lung and skin [see this *Bulletin*, 1959, v. 34, 790].

Aetiology and symptomatology of poisoning in animals and man precede a discussion of preventive measures and methods of detection. Protective clothing and canister masks are described, though workers directly exposed should have air-line respirators. Baths after work are advised and a 3% ammonia solution for washing clothing or contaminated skin. Periodic medical examinations should include liver function tests and estimations of serum proteins and non-protein nitrogen. In animals attempts at prevention or treatment with BAL, atropine, antihistamines and sedatives for diborane poisoning, and methylene blue for decaborane, indicate no practical solution, and the most stringent precautions to prevent contamination are as necessary in the laboratory as in the factory environment.

To demonstrate how much more dangerous the boranes may be than many chemicals used in industry, an American "Hazard Index" is reproduced in which Schechter [*ibid.*, 1958, v. 33, 949] gave indices for the boranes, hydrazine, carbon tetrachloride and benzene, and to this are now added indices for dimethylhydrazine and hydrocyanic acid. Diborane and pentaborane have indices greater than any of these substances and decaborane, a toxic solid, less because this useful index relates volatility to the rat 4-hour LC50.

M. Patricia Fitzsimons

Friede, R. L. **Subacute Boron Hydride Intoxication in Rats. Neuropathological and Histochemical Investigations.** *Arch. Indust. Health.* Chicago. 1959, Dec., v. 20, No. 6, 448–54, 3 figs. [16 refs.]

A decaborane compound, HEF-3, a high-energy fuel, 1 cc. being equivalent to 820 mgm. decaborane, was applied to the skin of rats to investigate changes in the central nervous system after absorption of sub-lethal amounts. Preliminary courses of 0·1 cc. daily and of other doses down to 0·012 cc. were fatal after several days. The doses were adjusted to maintain severe intoxication and to avoid cumulative effect. The usual sequence was 0·05, 0·05, 0·025, 0·025 and 0·01 cc., repeated after 2 days' rest and reduced if symptoms were severe, for 2 or 4 weeks. 3 of 30 rats died and the remaining 27 had almost identical reactions, even though absorption may have varied. They were killed on the last exposure day except 2 that were allowed to survive the 4-week exposure for 18 days. The brain and spinal cord were removed immediately, and these organs were also examined from 3 rats after 8 daily subcutaneous doses of 50 mgm. per kgm. or 6 of 79·4, within 11 or 8 days.

Intoxication developed in 3 stages: hyperexcitation with co-ordinated movements or twitching and aggressive behaviour starting in a few hours; depression, interrupted by agitation, accompanied by ataxy; coma. The first 2 stages were reversible. Convulsions occurred only after massive lethal doses. Repeated subliminal doses produced sudden intoxication after several symptom-free days.

Nuclei of nerve cells were enlarged; neurones with reduced chromatin or a disorganized chromatin pattern seemed more frequent than in controls; these scattered changes did not indicate permanent damage. Cerebral cortex sections are illustrated. There was a little fat in the grey matter, no abnormal deposition of glycogen and only minimal alteration in the distribution of protein and succinic dehydrogenase. Other organs were normal except for blood pigment deposition in the spleen and necrosis, extending into the corium, at the application sites. *M. Patricia Fitzsimons*

Von Oettingen, W. F. **The Aliphatic Acids and their Esters—Toxicity and Potential Dangers. The Saturated Monobasic Aliphatic Acids and their Esters.** *Arch. Indust. Health.* Chicago. 1959, Dec., v. 20, No. 6, 517–31, 2 figs. [Numerous refs.]

Khairy, M. **Changes in Behaviour associated with a Nervous System Poison (D.D.T.).** *Quart. J. Exper. Psychol.* 1959, May, v. 11, Pt. 2, 84–91, 1 fig. on pl. [21 refs.]

These experiments with rats were designed to show that behaviour could be used to investigate drugs which affect the nervous system. DDT was given with food, in doses of 100, 200, 400 or 600 p.p.m. daily for 21 days before and during 2 experiments which lasted several days.

In the first, problems in a closed field test were barriers and error alleys between the starting and food boxes. In phase 1, group and individual training took place until all animals completed trials quickly. In phase 2, problem-solving behaviour was studied; errors and times taken were recorded for different problems daily. In phases 3 and 4, with barriers re-arranged as a straightaway, the speed and pattern of locomotion were studied. Scoring for the pattern, which was run on charcoal paper, was calculated from the angle of gait; this is illustrated: the line joining the right paw-print to the left forms the hypotenuse of a right-angle triangle, the other sides being parallel to the paper edges; the tangent of the angle at each apex was calculated.

Problem-solving and speed were unaffected, but there was ataxia with a 2-fold action. The tangents from the lowest dose were very narrow. The mean was much below that of controls. The lowest dose exaggerated the stretch reflex, the others broadened the gait and shortened the steps. This test could detect chronic DDT toxicity in rats.

In the second experiment, reactions to stress, a light over the food, were studied in an open field test. The combined experimental groups showed less reaction than the controls, judged by scores from 7 types of response. Low urination scores particularly, and less markedly lowered rearing, preening and defaecation scores were noted. Previously reported hyper-irritability to stimuli was probably an exaggerated motor response; sensitivity to stimuli may remain unaltered.

M. Patricia Fitzsimons

FRADÀ, G. & GUCCIARDI, G. Effetti terapeutici nell'uomo del trattamento associato A.C.T.H., cloropromazina ed atropina nell'intossicazione da esteri fosforici. [**Therapeutic Effects in Man of Associated Treatment with Corticotrophin, Chlorpromazine and Atropine on Phosphoric Esters Poisoning**] *Med. d. Lavoro.* 1959, Nov., v. 50, No. 11, 645–58. [26 refs.] English summary.

The authors report 6 cases of poisoning by phosphoric esters, treated by a combination of corticotrophin, atropine and chlorpromazine. 5 of the patients were aged between 13 and 28 years, while 1 man was 65 years old. 2 patients had had mild toxic symptoms some days before the acute attack, 1 case was mild, but 3 were admitted to hospital in deep coma, while several of the patients had more or less marked symptoms of acute pulmonary oedema. None died. All the cases arose in the course of spraying work with E 605 or Olio-Phos, and 2 of the patients had eaten raw figs from trees which had been sprayed only a short time before.

In the combined treatment atropine was given as 1 mgm. every half hour till the appearance of mydriasis, corticotrophin intramuscularly up to 50 units twice daily, and chlorpromazine up to 10 mgm. every 2 hours for 24 hours (the treatment differed in each case). In 1 mild case corticotrophin was omitted, and the authors mention another 5 patients in whom only atropine and chlorpromazine were given successfully. They describe how once the acute attack had been survived, symptoms of a predominantly nervous type supervened; an effect on the kidneys was also noticed.

The authors point out that although atropine may counteract the muscarine-like effect it does not deal with the nicotinic-like action of these compounds and that if cholinesterase-reactivators like P2-AM are used atropine should be given as well. They are of the opinion, however, that their combined treatment proved very satisfactory. They suggest that poisoning by these phosphoric esters resembles a stress reaction which explains [to some extent] the favourable reaction of chlorpromazine. *W. K. Dunscombe*

EDSON, E. F. **Medical Assessment of the Organophosphorus Insecticide Diazinon.** *East African Med. J.* 1959, Dec., v. 36, No. 12, 661–4.

There is no evidence of toxicity to man.

WITTER, R. F. **Effects of DDVP Aerosols on Blood Cholinesterase of Fogging Machine Operators.** *Arch. Indust. Health.* Chicago. 1960, Jan., v. 21, No. 1, 7–9. [10 refs.]

"The levels of blood cholinesterases were studied in men who used Todd Insecticidal Fogging Machines to apply 4% 0,0-dimethyl-2,2-dichlorovinyl phosphate (DDVP) aerosols for 16 hours a week to tobacco warehouses. No decrease in the concentration of the plasma or red blood cell enzyme was found over a period of four months. It is concluded that this method of application of DDVP does not constitute a hazard to the health of these workers, providing the fogging machines are properly used."

WAGNER, G. Eine Analyse von 500 allergischen Kontaktekzemen. [**Analysis of 500 Allergic Dermatitides**] *Berufsdermatosen.* Aulendorf. 1959, Dec., v. 7, No. 6, 307–19, 4 figs. [19 refs.]

This is an account of 500 cases of contact eczema seen in a period of about 3 years in the Dermatological Clinic of Kiel University, in which the allergic origin of the skin condition was diagnosed by means of the skin patch test. Among the 500 patients there were 279 (55·8%) men and 221 (44·2%) women. In about 45% of all cases the allergic state was of industrial origin.

There is a considerable description of the difference between the sexes in regard to the allergizing materials. In men industrial materials accounted for 159 (57%) cases, medicaments for 98 (35·1%) and other allergens such as those in cosmetics, clothing and washing materials were numerically unimportant. Among women the picture was different for medicaments caused 109 (49·3%) cases, industrial materials only 31 (14%) cases but clothing caused 40 (18·1%) and cosmetics 25 (11·3%) cases.

In the industrial materials group of allergens, of which a list is given, the most frequent was cement containing hexavalent chromium salts, and next frequent were flour improvers containing persulphate. The most important in the medicament group were substances containing a para-amino group in the benzene ring, of which sulphonamides caused 41 cases. In the clothing group there were 22 cases of eczema caused by nickel buckles. Next in importance were dyestuffs, particularly those having a p-phenylene diamine grouping. The cosmetic group included cold wave preparations, hair dyes and other "make up" materials. The frequency of allergic skin conditions in different occupations is fully considered and an examination made of the diagnostic value of the skin test and the "standard test series" of materials used in the test at the Kiel clinic. *M. E. Delafield*

CARTER, T. C. **Radiation Exposure: Credit and Debit.** *Lancet.* 1960, Jan. 23, 217–18.

This is a serious attempt at striking a balance sheet between the gains to the population of X-ray exposures and the loss such people may suffer through genetic isomatic damage. The author draws attention to the fact that the benefits are more or less immediate whereas damage, especially if genetic, may not become apparent for many years and its connexion with the exposure is usually undemonstrable. So such damage constitutes a long-term debt to be paid eventually by somebody other than the borrower.

How can we estimate the magnitude of these debts? The most obvious way is to turn to the data which bring much damage home to us quantitatively.

In the Interim Report of the Committee on Radiological Hazards to Patients (London 1959) there are data derived from the findings in mass-miniature radiography of the chest during 1957. On the credit side comes the diagnosis of 41,597 conditions, including pulmonary tuberculosis, cardiac abnormalities, pneumoconiosis and lung cancer. On the debit side there is a maximum of 20 cases of leukaemia, possibly induced but yet to appear. The Report is incomplete owing to the absence of genetic data—the time interval was doubtless too small.

The relationship between the human mutation rate and radiation exposure is generally expressed in terms of the mutation-rate-doubling dose, *i.e.* the genetically effective radiation dose that would induce as much mutation per generation as arises spontaneously.

In the Report of the United Nations Scientific Committee on the effects of Atomic Radiation, New York, 1958, it was concluded that this doubling dose for man lies probably somewhere in the range between 10 and 100 rem. The author takes the latter figure in his subsequent evaluation of the component of the genetic debt due to single mutation-maintained genes incurred through any given exposure of the British population.

The broad result is that the numbers of defects occurring annually in the U.K. as a result of a continuing exposure to natural background radiation at an annual rate of 0·1 rem are as follows: Minor defects 591 cases; Major defects 299 cases.

For purposes of numerical perspective the number of births in the U.K. for that year was 851,466. With this quantitative line of argument in mind the author returns to the possible genetic damage in the mass-radiography series and it is abundantly clear that this debt is very small compared with the benefits already cited.

There are risks of damage from other sources of penetrating radiation; one is the general use of X-rays in medical radiology and the other arises from the contamination of the environment from radioactive waste disposal, reactor accidents, nuclear tests, etc.

From the further data given it is clear that continuing vigilance on the part of the authorities is the only way for national safety regarding radiation damage. *S. Russ*

MINISTRY OF LABOUR & NATIONAL SERVICE. H.M. FACTORY INSPECTORATE. **Radioactive Markers in Go-Devils: Safety Precautions.** *Safety, Health & Welfare, n.s. No. 7.* 13 pp., 2 figs. 1959, Mar. London: H.M. Stationery Office. [1s.]

Go-devils are types of equipment used by oil, gas, water and other industries to clear out or scour pipe lines. They consist of tightly fitted rubber washers, scraper vanes or wire brushes mounted on a central core. Compressed air or water pressure is used to push them through the pipe lines and sometimes they get stuck. The question is, where? The go-devils are now fitted with a radioactive marker housed in the central core—it is generally a sealed source of Cobalt 60, the gamma rays from which can be detected above ground. By an ingenious device this source is normally held inside a lead protective container which can be automatically removed when a finding test has to be carried out. The personnel has to be suitably protected during any such test; it means digging down to the spot indicated by a Geiger counter and all this time people are exposed to gamma rays from something of the order of 100 mc. ^{60}Co. The risks are not great, for the men on the job can be changed if it is unduly prolonged.

The paper contains detailed information about the maximum permissible levels of exposure to radiation with which employers must comply. *S. Russ*

SPALDING, C. K. & COWING, R. F. **A Survey of Radiation received by Dentists and Dental Assistants.** *Amer. Indust. Hyg. Ass. J.* 1959, Oct., v. 20, No. 5, 424–7, 2 figs. [13 refs.]

Although very little time is taken over an X-ray dental film, there is time enough for the exposed personnel to receive more radiation than is advisable, because the output from the X-ray tube is high.

Many dentists operate the X-ray machines themselves and remain in the same room as the patient, and inevitably they get a scattered dose; the same holds good for their assistants.

The authors found evidence that many practitioners did not conform to satisfactory standards of safety.

However, from the quantitative test carried out and described here it is seen that safety recommendations, if acted upon, result in a very sensible reduction of unwanted radiation. *S. Russ*

MORKEN, D. A. **The Radiation Dose to the Kidney of the Rat from Inhaled Radon.** *Arch. Indust. Health.* Chicago. 1959, Dec., v. 20, No. 6, 505–9. [14 refs.]

Radon is a poisonous gas although an inert one; this seeming contradiction is due to the fact that its poisonous character lies in the radiation it emits and to the active deposit it forms which can be no less damaging.

If pure radon enters the lungs it will diffuse rapidly and find its way into the blood stream, thence to the kidneys. During the whole of this journey active deposit is being formed and fractionally will remain *in situ* and constitute innumerable foci of radiation.

The author finds that damage to the kidney in rats follows their inoculation with a concentration of $1{\cdot}25 \times 10^{-4}$ curie per litre, maintained for $3\frac{1}{2}$ hours. Renal damage follows such exposures and by quantitative comparisons with the work of other authors it is shown that the kidney can be looked upon as a particularly sensitive organ to alpha rays. In particular it is important to bear this in mind in view of the Maximum Permissible Concentration for radon being based upon its effect upon lung tissue.

The author has some warrant for his suggestion that a safer basis of reference would be the damaged kidney. It is worth noting that so far no lung cancer has been induced in animals by submitting them to radon atmospheres. It may well be that the toxic action takes a toll of the animals before there has been time for tumour formation. *S. Russ*

SISEFSKY, J. **Method for Photographic Identification of Microscopic Radioactive Particles.** *Brit. J. Applied Physics.* 1959, Dec., v. 10, No. 12, 526–9, 3 figs.

"A method is described for identification and microscopy of small radioactive particles mixed with a large amount of inactive ones. The particles are prepared on a celluloid coating on a glass plate. The plate is coated with nuclear emulsion in gel form which is reversal developed *in situ* leaving the active particles visible, in the centres of clear circular spots against a brown transparent background."

MITCHELL, J. G. **Sensitive Detector of γ-Radiation in Liquid or Gaseous Effluents.** *J. Sci. Instruments.* 1959, Sept., v. 36, No. 9, 396–8, 4 figs.

STORY, E. J. **Control of Potential Radiation Hazard at the Raleigh Reactor.** *Amer. Indust. Hyg. Ass J.* 1959, Oct., v. 20, No. 5, 417–23, 6 figs.

The Raleigh Reactor in question is located at North Carolina State College. Initially (in 1953) it was operated at power levels below and near 10 KW.; this continued for 2 years when leaks were discovered in the wall of the stainless steel reactor vessel near the top of the core solution level. This happened before any risk could develop to the personnel. A simplified reactor was put into operation in 1957; this had only a power output of 500 watts. A higher powered machine is to be installed again.

Radiation hazards associated with these reactors are of two kinds, *viz.*: those from external sources of radiation and those from radioisotopes that might become airborne so that they could enter the body. The so-called external radiation leaks through the reactor shield or open beam holes or comes from irradiated material and radioactive waste.

These risks are easily met and the record at this site is proof of the efficacy of the precautions taken. There have been no exposures in excess of the maximum permissible dose of 300 mrem weekly. Internal hazards are more difficult to prevent because once a quantity of radioactive material has entered the body it is difficult to determine the resultant dose or to get rid of the material.

The author points out that radioactive poisons are more hazardous than chemical poisons by factors of about 10^6 to 10^9—chlorine, arsine, beryllium. The main sources of potential internal hazard are as follows:

(1) The handling and processing of materials activated by the neutron flux in the reactor.

(2) The effluent gases released during normal operations, mostly radioisotopes of krypton and xenon.

(3) At high power the argon and dust particles in the air surrounding the reactor may become activated.

(4) The probability that some time or other a leak will occur in the vessel holding the reactor solution. All of these matters are gone into detail in the text which is well illustrated with lay-outs and technical features.

There is no doubt whatever that work at this centre is most carefully planned and carried out. An illustration of this care is as follows: "It has been found that a safety officer or health physicist who is working for the people responsible for the experiments with the reactor or isotopes can have his judgment regarding safety somewhat biased. In fact, if his immediate supervisor desires to disregard certain precautions, it has been found that compromises, not always in the best interests of safety, will be made. For this reason the Campus Safety and Health Committee operates independently of any single department and hires a Campus Radiological Safety Officer who is responsible only to the Committee and the Chancellor".

Thus is assurance made doubly sure. For those who are planning work on these lines, there is much to be learned from this paper. *S. Russ*

HEATING, LIGHTING AND VENTILATION

BRITISH OCCUP. HYG. SOC. **Vision, Lighting and Colour. Papers read at 9th Conference on 11–12 Nov. 1958.** *Ann. Occup. Hyg.* London. 1959, Oct., v. 1, No. 3, 207–70, numerous illustrations. [25 refs.]

This symposium comprises 7 papers. In the paper on *Visual Perception* (pp. 208–216) Professor W. D. WRIGHT deals briefly with the acuity, light sensitivity and colour sensitivity of the visual system and with the role of saccadic eye movements in the dynamic process of vision. The discussion is concerned principally with the improvement of visual discrimination by training, the difficulties of colour-vision defectives and the time factor in seeing. The second paper, entitled *Subjective Aspects of the Evaluation of Lighting* (pp. 217–227), is by Dr. R. G. HOPKINSON. The author deals with subjective assessments of certain effects attributable to lighting, such as glare and visual comfort, but expresses some doubt whether it is worth while trying to integrate all assessments of this kind into a single index of the relative merit of different examples of lighting. Reference is made in the discussion to the wide variation between individuals in their sensitivity to glare. J. B. COLLINS contributes a paper on *Visual Fatigue and its Measurement* (pp. 228–236). He describes SOLDANHA's experiments showing the increase in errors made during 2-hour spells of exacting visual work but concludes that the test used is not suitable for general use. Variation in the time required for the act of lenticular accommodation is being studied as a possible index of fatigue due to seeing. The discussion indicates a sceptical view of the outcome of the author's current experimental studies. *Visual Tasks and Visual Capacities—their Rating and Mating* is the title of the paper given by R. J. FLETCHER (pp. 237–245). This author describes the analysis of practical visual tasks in terms of parameters such as the apparent size and contrast of the detail that has to be seen. Such characteristics determine the visual demands made by specific jobs and the visual capacities, *e.g.*, acuity, needed by the worker to match these demands and so to be able to perform the task efficiently and comfortably. The original paper and the ensuing discussion (pp. 245–248) should be read, since this important subject cannot be summarized adequately in the space available here. The fifth paper, by M. W. PIERCE, deals with some of the principal features in *Modern Methods of Artificial Lighting* (pp. 249–257). Emphasis is put on design for the visual comfort of the users. The subject of *Colour in Factory Buildings* (pp. 258–266) is dealt with by L. V. JONES. His paper is illustrated by a series of reproductions of colour photographs. The discussion of this subject is lengthy and covers a number of points, including colour preferences and the colour rendering due to different illuminants. The symposium is concluded with a contribution by J. G. HOLMES on *Lighting the Outdoor Factory* (pp. 267–270). The special problems involved are outlined and suitable lighting fittings and installations are described briefly with the aid of illustrations. The latter are, unfortunately, printed out of place with the discussion of the preceding paper. The papers in this symposium are necessarily selective in their treatment of subjects which already have a very extensive literature. They are, however, specially written for the information of all concerned with occupational hygiene and it is useful to have them collected in a single publication. *H. C. Weston*

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

Composition and Bacteriological Control

(i) MINISTRY OF HEALTH: MINISTRY OF AGRICULTURE, FISHERIES & FOOD. **Hygiene in the Retail Meat Trade.** *Food Hygiene Codes of Practice No. 1.* 19 pp., 1 fig. 1959. London: H.M. Stationery Office. [9d.]

(ii) ——. **The Hygienic Transport and Handling of Meat.** *Food Hygiene Codes of Practice No. 2.* 15 pp., 5 figs. 1959. London: H.M. Stationery Office. [9d.]

These two codes are issued jointly by the Ministry of Health and the Ministry of Agriculture and are advisory and not statutory. Each contains a number of sections, some of which are common to both.

I. This code has sections on construction, fittings and equipment and special sections dealing with offal cleansing, the storage and disposal of trade refuse, and the preparation and handling of meat products. Many of the suggestions made follow accepted lines but some paragraphs require notice. In para 1, the word "preferably" should have been omitted, as it inevitably gives the impression that the advice need not be taken. In paras. 22–24 the point is that for the same amount of light, fluorescent lighting is cheaper. Ventilating ducts (para. 25) should be fitted flush to wall and ceiling, as otherwise they become dust traps: (26), it is

to the proprietor's advantage that hot water pipes be lagged; in para. 31 wooden drainage boards should be discontinued. In paras. 48–50 no mention is made of the refrigerated display cabinet (see comment below), though admittedly the problem of the open meat stall in a market in the summer is extremely difficult. The cleanliness of trade-refuse containers cannot really be covered by a code of practice. As regards paras. 81–88 dealing with protective clothing, and safeguards against infection, see comment below.

II. Here sections include the construction of vehicles and their cleansing, loading and unloading, transport, and delivery, with again a section on personnel: In regard to para. 8 it is the reviewer's opinion that *studded* aluminium alloy flooring, if it is intended to transport sides or hind quarters of beef, would be very difficult to keep absolutely clean; in para. 23 once hessian cloth becomes soiled by meat it is practically impossible to get it clean enough by ordinarily available methods for re-use. The construction of suitable doors and tailboard is a difficult problem, as, while the roller shutter type is open to the objections mentioned, the fold-back type is too often left folded back; paras. 28–29, mechanical loading of vehicles is at present a rarity; para. 33, game, including both furred and feathered types, should be transported in a separate compartment; para. 48, dealing with carriers' vehicles points out the undesirability of such vehicles being used for carrying other goods at the same time. All are agreed on this but surely it should be possible to devise a way of ensuring that meat is carried *only* in vehicles properly constructed for that purpose. Para. 52 deals with protective clothing. The necessity for light coloured protective clothing with some form of satisfactory head covering for women is generally accepted, but the sanguinary head-gear worn by so many engaged in transporting meat is not exactly an advertisement for hygiene. The code could surely have suggested a plastic cap with long neck flap, and plastic coats which would be easily cleaned and look smart at the same time. These are now made for many industries so nothing new is involved.

[After some considerable experience, the reviewer must say that he feels that while such codes do no harm, because they are merely hortatory they do little good, and practical advice from the local Health Department is better than pamphlets. Many of the suggestions are covered by clean food bye-laws, a point completely omitted by the Minister of Health in his preface. Employers or proprietors must be shown that it is to their financial advantage to make improvements, and it is disappointing that the importance of glass refrigerated display counters and cabinets is not stressed as a selling line to impress the customer, who could in this way see what she wants to buy.]

W. K. Dunscombe

MINISTRY OF AGRICULTURE, FISHERIES & FOOD. **Food Standards Committee Report on Preservatives in Food** [WRIGHT, N. C., Chairman]. pp. v + 70. [Numerous refs.] London: H.M. Stationery Office. [4s. 6d.]

In 1951 the Food Standards Committee which wa set up in 1947 appointed the Preservatives Sul Committee with the following terms of reference: "T review the Public Health (Preservatives etc. in Foo Regulations and to make any recommendations the Sul Committee may consider desirable for the amendmen of the Regulations". The report on preservatives o the sub-committee was adopted by the Food Standard Committee and is presented here. In this report it mentioned that "Because of the wide range of sub stances covered by our investigations, we decided t report on each class of substance separately. Repor on antioxidants (1954) [this *Bulletin*, 1955, v. 30, 152 colouring matters (1954 and 1955) [*ibid.*, 1956, v. 3 555] and emulsifying and stabilising agents (1956) [*ibid* 1957, v. 32, 472] have already been published".

This is a valuable report containing a very grea amount of information which is clearly described an discussed. It is in 5 parts, in the first of which ther is a historical introduction and a statement of th general principles that "preservatives should only b employed in foods if their use has been expressl authorised; that additions should only be permitte where they have been shown to be necessary o advantageous, and then only in the amount needed t achieve the desired effect; and subject to the overridin requirement that the addition should not give rise t a health hazard". Part II contains proposals fo amending the general form of the preservatives regula tions. Part III is of particular medical interest in tha it contains a consideration of the properties of chemica preservatives and their possible effects on health, base chiefly on the advice of a Pharmacology Panel an an Antibiotics Panel. Modern knowledge and ex perience of the permitted preservatives—sulphurou acid, benzoic acid, nitrates and nitrites and dipheny are described and discussed. Preservatives some o which are allowed in other countries but are not a present permitted by the regulations are next considere at some length in respect of their properties, use an toxicity. They are sorbic acid, *p*-hydroxybenzoic acid esters, dehydroacetic acid, sodium diacetate, ethyl-*p* nitrobenzoate, ethylenediamine-tetra-acetic acid (EDTA) *o*-phenylphenol, vanillic acid esters, hydrogen peroxide nitrous oxide gas, propionic acid, boric acid and anti biotics. The use of antibiotics as food preservative is a recent development and is in use elsewhere. Chlor tetracycline and oxytetracycline are used for preservin poultry and fish; in the whaling industry chlortetra cycline is introduced into the body of the whale by th harpoon or the inflation pipe to prevent decomposition Nisin is used to preserve cheeses and certain canne foods. The conclusions of the Antibiotics Panel ar reported in an appendix.

In Part IV there is reported the full consideration which was given to the case for permitting preservative in a large number of individual foods.

A list of the large number of those who have sub mitted evidence or have been consulted is given in an appendix. Full references to the literature cited in Part III of the report are also recorded.

M. E. Delafield

BORNEFF, J. Fütterungsversuche mit Detergentien unter besonderer Berücksichtigung der Tbc.-Infektion. **[Feeding Experiments with Detergents in Relation to Tuberculous Infection]** *Arch. f. Hyg. u. Bakt.* 1959, Dec., v. 143, No. 8, 624–33, 3 figs. [17 refs.]

The problem of the possible dangers to health of the presence in food of foreign matters such as additives or of synthetic detergents which may gain entrance to foods has received considerable attention in the literature. The present paper is concerned only with detergents. These substances have no demonstrated direct toxic action in the doses usually ingested. These doses, according to the British and other literature on the amount of detergents in drinking water, do not amount to more than from 0·5 to 2·0 mgm. of surface active substance per person per day. The question of a possible indirect toxic effect of the prolonged daily intake of detergents by hastening the absorption of undesirable matters has not as yet been answered satisfactorily.

In previous work [*Arch. f. Hyg. u. Bakt.*, 1957, v. 141, 578] the author could find no evidence that detergents had any effect on the course of acute bacterial enteric infections. Here reported in detail are experiments on guineapigs to which tubercle bacilli of 2 strains were administered by injection or orally. A detergent (Hostapon or Pril) was given either by injection or by addition to the animals' food, either at the same time as or daily for 2 or 3 weeks before the bacillary injection. The course of the infection was observed by tuberculin testing and at autopsy. There is a description and discussion of the findings which provide no evidence that either of the surface active agents used in the stated amounts influence bacterial infections. Nevertheless, the problem of whether these agents "do or do not favour the resorption of cancerogenic substances" remains unsolved.

M. E. Delafield

FOOD POISONING

WILSON, G. S. **A Small Outbreak of Solanine Poisoning.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, Dec., v. 18, 207–10. [13 refs.]

This is an interesting account of a family outbreak of solanine poisoning, a condition which is very uncommon in Britain where the only notable record of it is of an outbreak involving 61 persons in Glasgow in 1917.

The present outbreak was in a family consisting of a hotel proprietor and his family of 4 persons who on 3 consecutive Sundays had cold meat with potatoes baked in their jackets for supper. The hotel proprietor who ate only the flesh of the potatoes remained well but the family, all of whom had consumed the skins as well as the flesh were taken ill on each of the 3 Sundays about 9 hours after the meal, with sickness, abdominal pain and diarrhoea. All the patients had recovered within 24 hours.

The potatoes were of excellent quality, had been imported from Israel and had been used in the hotel for some weeks without incident but had always been peeled before cooking. Analysis of potatoes from the same batch showed that they contained 50 mgm. of solanine per 100 gm.

The average content of solanine in potatoes is generally given as about 8 mgm. per 100 gm. The conditions under which it is formed in excess are not well defined but are discussed here with references to the literature. The highest content of solanine is found in those parts of the plant where metabolic activity is greatest, hence it is more concentrated in the sprouts than in the flesh.

The upper safe limit of solanine is given as 20 mgm. per 100 gm. There seems no reason to doubt that these outbreaks of illness were attributable to solanine poisoning

M. E. Delafield

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma; Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN

CANIZARES, O., SHATIN, H. & KELLERT, A. J. **Cushing's Syndrome and Dermatomycosis.** *Arch. Dermat.* 1959, Dec., v. 80, No. 6, 705–9. [23 refs.]

"Three cases of widespread and extensive dermatomycosis were observed among eight cases with Cushing's syndrome.

"This high incidence of generalized dermatomycosis among patients with Cushing's syndrome, in a geographic region where generalized tinea infections are rare, appears to be more than a fortuitous association.

"The dissemination of the fungus infection, due to T. rubrum in all our cases, is probably due to changes in the host immunity factor as a direct result of the

effect of the excess corticosteroids on the immunological defenses of the host.

"The presence of generalized dermatomycosis in association with unexplained hypertension, diabetes, or backache should make the clinician think of the possibility of Cushing's syndrome."

CHATTAWAY, F. W., TOWNSLEY, J. D. & BARLOW, A. J. E. **Effect of Steroids and Related Compounds on the Growth of Dermatophytes.** [Correspondence.] *Nature.* 1959, Nov. 28, v. 184, Suppl. No. 22, 1731–2.

Scattered literature regarding the possible influence of steroids and related substances on the course of mycotic disease stimulated the authors to investigate the direct effect of these substances on the growth of dermatophytes *in vitro.*

In this article they describe the results of some preliminary experiments. Commencing first with *Trichophyton rubrum* as the test organism, they inoculated flasks of fluid basal culture medium with the fungal suspension to which had been added 250 μgm. per ml. of one of the steroids or related substances. Results showed that some of these substances added in this manner to the culture medium were able to inhibit the growth of *T. rubrum.*

Subsequently, another experiment of a somewhat similar nature was carried out, but this time with the difference that several other dermatophytes besides *T. rubrum* were tested, namely, *T. mentagrophytes, Microsporum canis* and *Epidermophyton floccosum.* Results of this second experiment showed that the strongest inhibition of growth was produced by desoxycorticosterone acetate. Other substances such as cholesterol and cortisone had no inhibitory effect on the growth of these dermatophytes.

The authors conclude that the less polar acetates show a marked reduction in the power to inhibit the growth of dermatophytes. *C. J. La Touche*

KAFFKA, A. & RIETH, H. *Trichophyton mentagrophytes*-Varianten bei Laboratoriumstieren. [**Variants of *Trichophyton mentagrophytes* in Laboratory Animals**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 1, 96–106, 9 figs.

The English summary appended to the paper is as follows:—

"During an outbreak of dermatomycosis among rabits and guinea pigs four variants of Trichophyton mentagrophytes could be isolated. Three of them had the same macroscopic cultural appearance, but they differed in their microscopic morphology. The development of variants and the influence of the disease on it are discussed."

MERKEL, M. **Investigations on the Chemical Structure of the Genus *Achorion.* II. Chemical Structure of *Achorion quinckeanum.*** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 12, 501–5.

UTZ, J. P. & TREGER, A. **The Current Status o Chemotherapy of Systemic Fungal Disease.** *Ann Intern. Med.* 1959, Dec., v. 51, No. 6, 1220–29 [25 refs.]

"In actinomycotic infections, penicillin is still the most effective chemotherapy. Sulfadiazine in combination with an antibiotic is recommended in cases of nocardiosis. Iodides and vaccine therapy have been the major therapeutic measures recommended in cases of aspergillosis. Iodides are also standard treatment for sporotrichosis, geotrichosis and penicilliosis. There is little experience in the therapy of mucormycosis, and success has been achieved in a few cases by the surgical removal of the focus of infection, or by the control of an underlying disease, e.g., diabetes. In the treatment of histoplasmosis and blastomycosis, amphotericin appears to be effective. Amphotericin, similarly, seems to be the best drug thus far for cryptococcosis. Amphotericin is least effective in systemic coccidioidomycosis and candidiasis, but worthy of use in the absence of other, effective chemotherapy."

JOHNSON, R. W. & SCHERAGO, M. **The Effect of Histoplasmin *in vitro* on the Migration of Leukocytes from Guinea Pigs experimentally infected with *Histoplasma capsulatum.*** *Amer. Rev. Respiratory Dis.* 1960, Jan., v. 81, No. 1, 96–9.

"The leukocytes of guinea pigs experimentally infected with about 10,000 living yeast-phase cells of *Histoplasma capsulatum* have been found to develop significant specific sensitivity, *in vitro,* to a 1:1,000 dilution of histoplasmin.

"Skin sensitivity first appeared in the infected animals during the third week after infection, while inhibition of leukocyte migration appeared as early as the second week in 2 of 4 animals tested. After the fourth week the migration of leukocytes from all of the infected animals was inhibited. Both skin and leukocytic sensitivity persisted through the ten-week period of the study. Consistent significant sensitivity was not found with the 1:5,000 or 1:10,000 dilutions of histoplasmin. The sensitivity was considered specific since brucellergen had no significant inhibitory effect on the migration of the leukocytes from the infected animals."

CARETTA, G. Caratteristiche morfo-biologiche di ceppi fungini del genere *Geotrichum* isolati da materiale umano. [**Morphological and Biological Characteristics of Strains of *Geotrichum* Isolated from Man**] *Mycopathologia.* The Hague. 1959, Oct. 15, v. 11, No. 3, 217–37, 12 figs. on 2 pls. [33 refs.]

A detailed morphological and biochemical study of 12 strains of *Geotrichum* isolated from human stools was carried out by the author.

It was found that these strains were, on the whole, uniform from a morphological standpoint, especially when they were grown on corn-meal agar. The mycelium consisted of dull and hyaline segments, branches arising indifferently from either. The arthrospore was the end process of hyphal differentiation. It was initiated by the appearance of a transverse

pseudo-septum of denser protoplasm which on lysis isolated the arthrospore. Glucose was assimilated by all the strains; saccharose by 8; galactose by all; lactose by only 2, raffinose by 5 and maltose by 9. All strains assimilated nitrogen well in the form of peptone, whereas nitrogen presented in KNO_3 was assimilated by all but to a less degree. All the strains were referable to *Geotrichum candidum* Link ex Persoon.

C. J. La Touche

KOZINN, P. J., BURCHALL, J. J., TASCHDJIAN, Claire L., WIENER, H. & NUMEROF, P. **Preparation of P^{32}-Labeled** *Candida albicans*. *J. Dis. Children.* Chicago. 1959, Dec., v. 98, No. 6, 765–7.

Since little is known regarding the mode or route of the transmission of pathogenic organisms from one host to another it occurred to the authors that some information could be gained regarding this problem through the use of radioactively labelled organisms in experimental work. The organism selected was *Candida albicans* and this was labelled with radioactive phosphorus.

C. albicans was cultured in Sabouraud broth containing radioactive phosphorus. After being thoroughly washed and checked for radioactivity the organisms were subcultured to non-radioactive Sabouraud broth.

Subsequently, tagged and non-tagged strains were studied and compared with regard to "growth rate, microscopic morphology, chlamydospore formation, fermentation reactions and animal pathogenicity". No differences were observed in the results obtained.

Radioactivity as measured by autoradiographs was still present at the 4th subculture but diminished "in a straight-line progression", none being detectable in the last 2 of 6 subcultures.

Radioactivity could be detected over a period of 8 days in sections made from experimentally induced lesions in mice when labelled inoculum was used.

The transmission of a tagged strain of *C. albicans* could be traced from the maternal vagina of mice to their newborn offspring [see below].

C. J. La Touche

KOZINN, P. J., TASCHDJIAN, Claire L., BURCHALL, J. J. & WIENER, H. **Transmission of P^{32}-Labeled** *Candida albicans* **to Newborn Mice at Birth.** *J. Dis. Children.* Chicago. 1960, Jan., v. 99, No. 1, 31–4. [12 refs.]

In pursuance of investigations which the authors have previously reported [above] a strain of *Candida albicans* freshly isolated from a human patient with oral thrush was used to induce infection in mice.

This strain was transferred to and maintained on Sabouraud agar containing radioactive phosphorus. Before its use for inoculation purposes it was washed until it gave a negative Molisch reaction for carbohydrates. The sediment of a centrifuged sample was then pipetted into the vagina of mice. Inoculation was repeated at 24-hour intervals as it was found that the organisms were shed every 12 hours during the stage of dioestrus which prevails in pregnant mice.

Litters of newborn mice "were killed within less than 24 hours after birth, preliminary experiments having shown that *C. albicans* does not establish itself in the newborn mouse and is eliminated within 48 hours".

Cultures were made from the mouth, gastro-intestinal tract and skin of these newborn mice, and in 39 out of 57 mice radioactive *C. albicans* was isolated from some or from all of these sites.

According to the authors, these results suggest that human infants become infected while passing through the vagina of the mother at birth and that *C. albicans* establishes itself either in the mouth or the gastro-intestinal tract which may in turn provide a nidus of infection for the napkin area. *C. J. La Touche*

MANCHESTER, P. T., Jr. & GEORG, Lucille K. **Corneal Ulcer due to** *Candida parapsilosis* (*C. parakrusei*). *J. Amer. Med. Ass.* 1959, Nov. 7, v. 171, No. 10, 1339–41, 1 fig.

This is an interesting account of fungal infection of the cornea of the right eye in a woman aged 37 years who was suffering from superficial punctate keratitis of the left eye and was receiving bacterial antibiotics and steroid therapy.

The patient had a small central corneal ulcer in one eye, and was treated with atropine, sulphamethizole and oral chloramphenicol. A few weeks later hypopyon developed; cultures were sterile for bacteria, but the ulcers remained, and eventually yeast colonies were obtained on Sabouraud dextrose agar at 25°C. and identified as *Candida parapsilosis*. Nystatin and potassium iodide were prescribed, and amphotericin B was used for eye drops, but there was no improvement until sulphacetamide drops and nystatin drops were used. This treatment was eventually successful.

In the course of their discussion of this case the authors emphasize the necessity for establishing the presence of the suspected fungus in scrapings from the lesion, a requirement which had not always been fulfilled by previous recorders of analogous cases.

Previous cases of fungal infection of the cornea cited include species of fungi belonging to 8 different genera of the *fungi imperfecti*. *C. J. La Touche*

HEINRICH, S. Zur Aetiologie und Mikrobiologie der Aktinomykose. IV. Über die Empfindlichkeit des *Actinobacillus actinomycetem-comitans* gegen die gebräuchlichen Antibiotica und Sulfonamide *in vitro*. (Ein Beitrag zur antibiotischen Therapie der Aktinomykose des Menschen.) [**On the Aetiology and Microbiology of Actinomycosis. IV. The** *in vitro* **Sensitivity of** *Actinobacillus actinomycetem-comitans* **to usual Antibiotics and Sulphonamides**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 2, 255–63.

The English summary appended to the paper is as follows:—

"Former papers proved the 'poly-bacterial' etiology

of human actinomycosis. Especially Actinobacillus actinomycetem-comitans has a major influence on the outbreak and course of this disease. Thus, the composition of the bacterial flora of actinomycosis has to be considered when antibiotics and sulphonamides are selected for therapeutic use.

"A number (10 to 37) of strains of Actinobacillus actinomycetem-comitans were tested for their in vitro sensitivity to therapeutic antibiotics and sulphonamides using dilution and diffusion tests.

"Within the limits of blood levels obtained all strains were sensitive to tetracyclines. The strains tested differed in their sensitivity to streptomycin, chloramphenicol and, especially polymyxin B.

"All strains were resistant to penicillin, oleandomycin, selectomycin and, with a few exceptions, to erythromycin.

"The diffusion test (disc test) proved to be useful as a routine test of the sensitivity of Actinobacillus actinomycetem-comitans providing a quick possibility to check the therapy."

YOUNG, Barbara B. & HOTCHKISS, Margaret. **Developmental Morphology in the Genus** *Nocardia*. *Mycopathologia*. The Hague. 1959, Nov. 30, v. 11, No. 4, 297–310, 45 figs.

Identification of aerobic actinomycetes is always difficult especially by morphological criteria.

The authors, using the microculture technique described by MCCLUNG (*Lloydia*, 1949, v. 12, 137; *J. Bacteriology*, 1950, v. 59, 589; *Ann. New York Acad. Sci.*, 1954, v. 60, 168) inoculated hanging drops and agar blocks on microscope slides with 6-week-old cultures of *Nocardia asteroides*, *N. brasiliensis*, and *N. madurae*. Cover-slips were deposited on top of the agar blocks.

The growth of these organisms was followed daily, and when morphological changes were observed a culture was fixed, stained and photographed. A series of photographs thus obtained illustrates these changes over a 6-week period and are reproduced with the article.

"The branching filaments of *N. asteroides*" produced an abundance of coccoid bodies and these then germinated to form branching filaments. "In *N. brasiliensis* branching filaments" fragmented into bacillary elements that stained deeply and sometimes contained granules. In *N. madurae* parallel hyphate were produced in young cultures and in older cultures "attached terminal coccoid or club-shaped bodies as well as swellings in the hyphae." *C. J. La Touche*

BOJALIL, L. F. & CERBON, J. **Schema for the Differentiation of** *Nocardia asteroides* **and** *Nocardia brasiliensis*. *J. Bacteriology*. 1959, Dec., v. 78, No. 6, 852–7, 2 figs. [10 refs.]

The usual tests applied to the differentiation of *Nocardia* species such as colonial morphology and sensitivity to chemotherapeutic agents are, in the opinion of the authors, not sufficiently reliable because of the great variability exhibited by species of this genus.

The aim of this study was to provide reliable physiological criteria whereby the 2 species, *Nocardia asteroides* and *N. brasiliensis* could be distinguished from each other.

68 variously named strains of *Nocardia* originating from a number of different sources were studied. They were grown in a culture medium consisting of: gelatin 4·0 gm.; distilled water 1,000 ml.; *p*H 7, and distributed in 5 ml. portions in test-tubes.

In this medium various strains could be divided into 2 metabolic groups represented by *N. asteroides* on the one hand and *N. brasiliensis* on the other. Thus, those which could be included in the first group (represented by *N. asteroides*), grew very poorly, developing a thin flaky type of growth which could be easily dispersed in the culture medium which became acid or remained neutral, while the ninhydrin reaction was negative; and lastly, the substrate was not utilized by these strains. Those which could be included in the second group (represented by *N. brasiliensis*) developed spherical colonies on the surface and wall and bottom of the culture tube; their culture medium became alkaline, while the ninhydrin test was positive in this medium and lastly the substrate was utilized. *C. J. La Touche*

NEILSON, D. B. **Pulmonary Aspergillosis associated with Radiation Pneumonitis.** *Scottish Med. J.* Glasgow. 1959, Dec., v. 4, No. 12, 557–62, 10 figs. [21 refs.]

This is a description of a case of *Aspergillus* infection of a bronchogenic cyst following exposure to therapeutic X-rays.

The patient was a woman aged 57 years who, when seen, gave a history of respiratory infection of 3 weeks' duration. 18 months previously a right mastectomy for scirrhus carcinoma had been performed and this had been followed by daily irradiation.

Before radiotherapy a routine X-ray had revealed a large thin-walled cyst in the right lung. The patient was febrile although the sputum did not contain tubercle bacilli. Antibiotics were without effect on the pyrexia.

3 weeks later a lower lobe lobectomy was performed. On examination this was found to contain a cavity measuring 6 cm. in diameter. It was lined by "greyish white shaggy, friable material". Fungal elements were numerous and lay free in the cavity in necrotic débris as well as in abscesses which were deeply seated in the cavity wall. They were absent from the adjacent lung parenchyma or nearby inflamed bronchi.

Cultures from the sputum yielded *Aspergillus fumigatus*.

It is suggested by the author that "pneumonitis produced by radiation so devitalised the lung and especially the epithelium lining the cyst as to allow the growth of inhaled spores of the Aspergillus". *C. J. La Touche*

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN.

TUBERCULOSIS

CHALKE, H. D. **Some Historical Aspects of Tuberculosis.** *Pub. Health.* 1959, Dec., v. 74, No. 3, 83–95. [35 refs.]

After a glance at the history of tuberculosis as a disease of the famous figures in literature, painting and music, and at the possibility that the illness itself may have contributed something to the intellectual qualities of the geniuses who suffered from it, the author goes on to set out his view that in Britain we have come towards the end of a long epidemic wave which probably began early in the 18th century, reached its peak in the 19th and began to subside considerably before control schemes were put into operation. The epidemic was fostered by the industrial revolution, when in spite of much prosperity there was gross poverty, and life was cheap. He quotes instances of enormous death rates from tuberculosis in small communities in which records were kept, and comments on the still apparent susceptibility of certain racial groups whose communal experiences of the disease has not been so drastic and who have therefore not passed through so severe an evolutionary phase of selection—though he puts it that they have "not yet acquired that increased resistance which long years of racial infection should bring about".

Other communities in developing countries may go the same epidemic way, but it was a hard and disastrous way, and perhaps it can be avoided.

Charles Wilcocks

NORTHERN IRELAND TUBERCULOSIS AUTHORITY [CHRISTIE, D. H., Chairman]. **Thirteenth Annual Report Year ended 31st Day of December, 1958 and Final Report Period ended 31st Day of March, 1959.** pp. xiv + 59, 3 graphs (1 coloured); pp. iv + 5. 1959. Belfast: 27 Adelaide Street.

This is the final report of the Northern Ireland Tuberculosis Authority, as on the 1st April, 1959, it was dissolved, and its functions transferred to the Northern Ireland Hospital Authorities, and the County and County Borough Health and Welfare Committees. [Some authorities think that this was premature and might have been postponed until tuberculosis was shown to be more fully under control than it is at present.] The report gives a full account of the various activities of the Authority.

Among the interesting features of the report are the following:

In the mass X-ray service, the number of active post-primary cases discovered among those sent by general practitioners was equivalent to 1·11% of the persons examined, compared with 0·20% for the mass radiography serivce as a whole.

Vaccination against poliomyelitis led to a catastrophic fall in the number of school leavers vaccinated with BCG. There was a fall of 39% and 37% in County Antrim and County Down respectively. The tuberculin reactor rate in school leavers continued to decline, being 21% compared with 25% in 1957. Notifications morbidity rate was 84 per 100,000 compared with 83 in 1958. This was due to an increase in the number of non-respiratory cases notified. It suggests a more complete notification of this form of the disease.

Death rate for respiratory cases was 9·91 per 100,000 and for non-respiratory cases 1·07. This is a new record low level for Northern Ireland.

A graph showing the mortality from all forms of tuberculosis in 1906 to 1958 shows that the mortality has dropped in Northern Ireland far beyond that of Scotland or Eire, though it is still above those in England and Wales. The death rate from tuberculosis among men was more than twice that reported among women. Numerous statistical tables are appended.

Among the operations, thoracoplasty seems still relatively popular. 47 thoracoplasties were performed against 74 resections of various types.

It is rather surprising that out of 271 children admitted for observation, no less than 70 were detained in hospital for 6 months or more, and still discharged as being under observation.

[For the purposes of comparison it seems rather a pity that the Northern Ireland Tuberculosis Authority was dissolved. It would have been very interesting to observe the results of the anti-tuberculous campaign carried out under an authority of this kind compared with the scheme at present in vogue in Great Britain.]

F. H. Young

TINKER, Cecily M. **Pulmonary Tuberculosis among Men over Forty.** *J. Hygiene.* 1959, Dec., v. 57, No. 4, 367–85, 2 figs. [44 refs.]

It has been known for some time that whereas the notification rate in cases of pulmonary tuberculosis in England and Wales has fallen rapidly both in young women and young men no such fall has taken place in the notifications for men over 45, which show a decline of only 1% between the years 1952 and 1956. The same applies to the mortality rate which for men of over 65 was 640 per million in 1956, compared with 14 per million for men aged 20–25. This has not been observed in the case of women. Both the male mortality and morbidity rates exceed the female rates

throughout England and Wales, in both the male excess is greatest in the large towns and least in the rural areas. In the rural areas the pattern of male mortality most closely resembles the female pattern. Both SPRINGETT [this *Bulletin*, 1951, v. 26, 1064; 1952, v. 27, 124, 638] and LOWE [*ibid.*, 1955, v. 30, 578; 1957, v. 32, 238] in separate papers show that much of the mortality among older men is due to reactivation of tuberculous disease acquired, but not diagnosed, in adult life.

In this paper a study is made of those factors already known to bear unequally on men and women and to be more prevalent in urban environment. This included the employment of men in large groups exposing them to risk of infection and superinfection at work, from which women over 40 are largely protected by marriage; conditions of employment among men from which women are protected by factory legislation; the influence of social habits known to be more prevalent among men than women, and in urban than in rural groups, namely smoking, alcoholism, and casual employment which involves moving from town, and sleeping in lodgings and lodging houses; also the association with other illnesses known to be more prevalent in men than women, and in urban than in rural surroundings, namely peptic ulceration, chronic bronchitis, and pneumonia.

Workers in the Civil Service were investigated to decide whether employment among women had any deleterious effect but although the relatively small number of women at risk makes the results obtained unreliable there was no evidence that the incidence of tuberculosis among women employed in the Civil Service was higher than the national average. Clinic figures were examined to see whether areas containing a lodging house had a higher proportion of cases of pulmonary tuberculosis than areas which had not; there was a difference, but hardly significant. As regards associated illnesses, peptic ulceration was the only condition which showed a significantly larger proportion of cases of tuberculosis in the older age-group. Neither over-time working, night work, nor self-employment in small businesses suggests that under present conditions in London these factors have any importance. In the following groups tuberculosis was more prevalent: Scots, Irish, Welsh, or foreign nationality, people who were single, widowed or divorced, residents in common lodging house or hostels, people with inadequate or special diets, heavy drinkers and smokers, and those who had insufficient sleep.

It is tentatively concluded that the casual workers of an urbanized community are one of the principal reservoirs of tuberculous infection in large towns. This interesting study is illustrated by a wealth of statistical tables. *F. H. Young*

VALLEGIANI, L. Rilievi clinico-statistici sulla tubercolosi di primo accertamento in Tripolitania. [**Clinical-Statistical Observations on Tuberculosis diagnosed for the first time in Tripolitania**] *Lotta c. la Tubercolosi.* 1959, Sept., v. 29, No. 9, 1256–66, 1 graph. [14 refs.]

At present there is only one dispensary or tuberculosis clinic to serve a population of 700,000 in the city of Tripoli and in Tripolitania: 2 outlying sub dispensaries were closed down in 1955. From th records of this Tripoli centre the author has extracte and tabulated annual figures, covering the period o 1948–58 inclusive, to show:

(a) total number of attendances and examinations;
(b) number of first visits;
(c) number of new cases of tuberculosis found eac year;
(d) (c) as a percentage of (b);
(e) percentage of patients with ulcerating, caseating diffuse or otherwise serious lesions giving a ba prognosis;
(f) percentage of those with only hilar involvemen or other early lesions amenable to successfu treatment.

Vallegiani gives a graph on which he has plotte curves for (a), (b), (c) and (e) to show that the firs 3 have been rising and (e) has been falling in the las 2 or 3 years of the 11-year period. Total attendance were 2,670 in 1948 and 14,532 in 1958, first visits wer 883 and 5,367 respectively, rates of positive diagnose 36% and rates of cases with a bad prognosis 85% and 48%. For 1958 he has classified the 1,388 case into 14 forms according to a standard terminology. The sex distribution shows a higher proportion o serious cases among the women, which is understandi able in a Muslim Arab country where the standards o public health are not high. Miniature radiography wa expected to become available soon to help early diag nosis. The author discusses the importance, as an index of the effectiveness of anti-tuberculosis measures of the ratio between (b) and (c) and between (f) and (e) above. *J. Cauchi*

ANN. SOC. BELGE DE MÉD. TROP. 1959, Aug. 31, v. 39 No. 4 *bis*, 531–629. [11 refs.] Colloque sur la tuberculose, Léopoldville, 30 janvier-3 février 1959 [**Conference on Tuberculosis, at Léopoldville 30 January to 3 February 1959**]

This special issue of the *Annales* is entirely taken up with an account of the conference, written as a continuous narrative of the proceedings, except that 4 papers by individual authors are printed in full after the account of the third day's work and before the recommendations and conclusions.

The first day was devoted to diagnosis, and details are given of the techniques of the tuberculin and BCG tests, of mass radiography and of the classification of the various forms of tuberculosis found. Prevention was discussed, and there were comments on isolation BCG, chemoprophylaxis and education.

On the second day the conference discussed treatmen in hospital and in out-patient conditions.

On the third day the subjects included social measure and the question of extending the campaign throughou the country.

These sections of the report, and the recommendations and conclusions, seem to be agreed statement issued from the conference as a whole. The 4 paper by individual authors are rather different, embodying their own opinions. The first is by J. ANDRE and A. VAN HERREWEGE (pp. 580–600) and in it the author

argue that the BCG test with killed organisms is more sensitive and more specific than the Mantoux test with 100 TU. For diagnosis they point out that each hospital directed by a doctor has its own X-ray apparatus, and that diagnosis by sanitary inspectors and medical assistants in the more remote areas usually depends on physical and sputum examination. Details are given of patients treated in the sanatorium at Mosango, where surgical procedures are carried out. The techniques used for administration of BCG are described.

J. HALET (pp. 601–603) briefly discusses ambulatory treatment of 284 seriously ill patients in Elisabethville; they had usually been in hospital for a period beforehand. Streptomycin, PAS and isoniazid were used, and he reports 12% patients dead, 13% incurable and 75% in whom good results were obtained. K. SEGHERS (pp. 605–612) writes in general terms on surgery in pulmonary tuberculosis.

J. TENRET (pp. 613–618) has attempted to assess the value of BCG administered in 1955 to the tuberculin-negative persons in a community of 62,369 (80–97·75% conversions) with revaccination one year later in those who reverted to negative. Another community of 36,495 was taken as a control. The incidence of tuberculosis in these 2 communities before vaccination, and calculated on the basis of X-ray examination of 49,790 persons, was 10·46 per 1000. Re-examination by X-ray of 33,462 from the vaccinated community 3 years later showed an incidence of 4·54 per 1000, whereas in the unvaccinated community (12,662 examined) it had risen slightly, to 11·29 per 1000. Thus in comparison with the known incidence before vaccination, and with the control community, the incidence in the vaccinated community had been more than halved. These figures relate to the whole population groups, but when only the actual persons vaccinated are reviewed, it is found that the incidence in them (28,191 persons) was only 0·17 per 1000. The vaccine used was lyophilized, and was carefully handled; the author emphasizes the necessity of revaccination, preferably each year, for those in whom the allergic state has declined.

This publication ends with a series of recommendations and conclusions. Advice is given on tuberculin testing (Mantoux 10 TU), BCG testing and mass radiography (with a system of classification). Isolation of tuberculous persons is regarded as important, but isoniazid prophylaxis is not advocated for persons who have recently become tuberculin positive, unless they show other evidence of disease (but it may be used in child contacts.)

BCG is strongly recommended, the intradermal route being preferred, and there is agreement that it could be administered without previous tuberculin test if trials in small groups of people show that this was innocuous. Health education is mentioned.

For treatment in hospital streptomycin, PAS and isoniazid are advocated, and other conventional drugs, and corticosteroids, are also used, with the possibility of surgery in appropriate cases. For ambulatory treatment (after 6–9 months in hospital if possible) streptomycin should be given daily, or 2–3 times each week, and isoniazid should be continued.

The social measures advocated include public assistance for the families of sick persons, and special funds for the tuberculosis campaign. For incurable and infective persons the possibility of special isolation villages is mentioned. *Charles Wilcocks*

WILCOCKS, C. **An Analysis of Some Recent Work on Tuberculosis in Africa.** *Brit. J. Dis. Chest.* 1960, Jan., v. 54, No. 1, 31–9. [70 refs.]

This challenging and authoritative analysis by one who was himself actively engaged in tuberculosis work in East Africa at one time is based on a large number of papers many of which have already been noticed in this *Bulletin*. The facts about tuberculosis in Africa are well known but there is still need for discussion on their interpretation and the lessons to be drawn from them.

There is ample evidence that environment is more important than heredity in the African's experience of tuberculosis. A high incidence of acute disease will be seen in the slums of industrial areas but not in the rural areas where tribal life pursues its quieter pace and a chronic type of tuberculosis may be seen.

Chemotherapy is being brought to Africa increasingly with beneficial results, and surgery accompanies it. In the absence of sufficient tuberculosis hospitals and dispensaries out-patient or domiciliary treatment is widely used. A course of isoniazid and PAS for 6 months has been found capable of influencing the great majority of non-fibrous lesions, and if streptomycin is added 90% of all lesions may be treated satisfactorily. If isoniazid is used alone drug-resistance is likely to become as serious a problem in Africa as elsewhere.

BCG vaccination has been used very widely in the French territories of Africa and in the Belgian Congo but only on a small scale in the British territories. Statistically valid trials cannot of course be made but the trend of the evidence is favourable to BCG.

Wilcocks emphasizes that the control of tuberculosis will be achieved by improving the environment through fundamental public health measures assisted by specific measures to find, isolate and treat and by BCG vaccination. If fair wages and acceptable working conditions are not accompanied by the provision of decent and healthy living conditions for workers and their families tuberculosis will remain in possession.

H. G. Calwell

KATZ, J. & KUNOFSKY, S. **Environmental versus Constitutional Factors in the Development of Tuberculosis among Negroes.** *Amer. Rev. Respiratory Dis.* 1960, Jan., v. 81, No. 1, 17–25, 1 fig.

The data presented in this discussion of the above problem were obtained since 1941 in the mental hospitals of New York State. All patients are X-rayed on admission and routinely thereafter. Patients with active tuberculosis are segregated and treated in special centres.

For purposes of comparison it was estimated that in the general population of New York City from 1943 to 1955 tuberculosis case rates were about 4 times as

high for Negroes as for whites. In contrast there was a difference of about 50% between the races in the mental hospitals, which difference declined to about 30% in the latter period of observation. The incidence fell more rapidly among Negroes than among whites.

The difference in incidence was partly due to the fact that the Negro patients are younger than the white patients. When the rates were adjusted for age the excess among Negroes was found to have dropped to 8% at the end of the period. A similar adjustment would have little effect on the 4:1 ratio in the general population.

Among those who developed tuberculosis the proportion who died of the disease was similar in both races. Antimicrobial drugs benefited both races similarly. It was therefore concluded that the response of the Negro to tuberculosis is mainly determined by his environment and that racial factors play a minor role in producing differences in morbidity and mortality between the Negro and white races in the United States.

H. G. Calwell

MACKAY-DICK, J. **Tuberculosis among the Gurkhas and their Dependants serving with the United Kingdom Forces in the Far East.** *J. Roy. Army Med. Corps.* 1960, Jan., v. 106, No. 1, 28–36.

Gurkha troops recruited in Nepal serve with the British army in Malaya, Singapore and Hong Kong.

All recruits have their chests X-rayed on entry and are tuberculin tested (Heaf test). Non-reactors are vaccinated with BCG. After tuberculin conversion all those vaccinated are retested and X-rayed annually for 5 years. Natural reactors are X-rayed every 3 years provided they do not subsequently become contacts of persons with notifiable tuberculosis. All soldiers are X-rayed immediately before and after their triennial leaves to Nepal.

All infants aged 3 years and under who are found to be reactors (Heaf test), in the absence of evidence of active disease, are given chemoprophylaxis.

On the diagnosis of tuberculosis notification is made to various officials and contact examination on a wide scale ensues. Contacts with normal skiagrams are also tuberculin tested and the X-ray examination is repeated every 3 months for 2 years, every 6 months for the next 2 years and then at the end of the 5th year after contact. Full records are kept. 3 army mass radiography units tour the areas examining troops, families and locally employed civilians.

The Gurkha sanatorium in Malaya includes accommodation for women; 146 beds were occupied in 1956. The standard treatment is daily streptomycin and isoniazid for 60–90 days and thereafter every 2nd day for a total period of 24 months. Soldiers for whom operative treatment is prescribed are sent to the United Kingdom. Every effort is made to return men to their regiments.

Pregnant women with tuberculosis are treated throughout their pregnancy. Infants are isolated from them at birth and vaccinated with BCG.

H. G. Calwell

CHINESE MED. J. Peking. 1960, Jan., v. 80, No. 1, 62–7. **Prevention and Treatment of Tuberculosis in China** [ANTITUBERCULOSIS ASS. OF CHINA, Peking].

According to this paper very little anti-tuberculosis work was done in China until its liberation in 1949 when "New China" began to advance under the leadership of the Chinese Communist Party.

In 1949 there were in the whole country 12 establishments with less than 100 doctors and about 600 beds for tuberculous patients. Now there are 236 establishments with over 35,000 beds. In addition 10% of beds in general hospitals are assigned to tuberculosis patients and there are 5,000 beds in workers' health resorts. There are over 2,700 doctors and "feldshers" in tuberculosis institutions.

The Ministry of Health directed that prevention and treatment should first be made available for industrial workers and the personnel of state schools and organizations and extended by degrees to rural areas. The "patriotic health campaign" has stimulated anti-tuberculosis work, and much use has been made of posters, films and radio.

Before "liberation" the incidence of tuberculosis in some of the large cities was 3–9% and the death rate in Peking was 230/100,000 in 1949. These figures were 1·0% and 46 respectively in 1958.

Modern chemotherapy and antibiotics are used along with traditional Chinese drugs and acupuncture. The last 2 measures have been found beneficial in conditions described. Collapse therapy and surgical treatment are used widely. Over 17 million persons have been vaccinated with fresh or freeze-dried BCG vaccine. The results are said to be good.

The decisive factors in the advances made are said to be the social factor, the general participation of the masses of the people in health work and lastly the advanced experiences of the Soviet Union. The authors are confident that under the leadership of the Communist Party they will before long rid China of tuberculosis.

H. G. Calwell

RILEY, R. L., MILLS, C. C., NYKA, W., WEINSTOCK, N., STOREY, P. B., SULTAN, L. U., RILEY, M. C. & WELLS, W. F. **Aerial Dissemination of Pulmonary Tuberculosis. A Two-Year Study of Contagion in a Tuberculosis Ward.** *Amer. J. Hyg.* 1959, Sept., v. 70, No. 2, 185–96, 1 fig.

A hospital ward occupied by tuberculous patients was ventilated by a closed system, the exhaust duct of which led to a chamber containing healthy guinea-pigs [this *Bulletin*, 1957, v. 32, 801; 1958, v. 33, 449].

During a period of 2 years the total number of animals exposed was 373 of which 156 were in the chamber at any one time; 71 were infected. The number of sputum-positive patients occupying the ward during any 1 month varied from 3 to 6.

Infection did not occur evenly; the number of infections acquired during the course of a month varied

from 0 to 10 (average 3), and there were 4 consecutive months when no animal became infected. This coincided with the presence of patients undergoing initial chemotherapy; their strains of tubercle bacilli were drug-sensitive. There is a possibility that the viability of the tubercle bacilli in the air-borne state was reduced in these circumstances.

At autopsy single primary pulmonary tubercles were usually found. Identification of the patient who infected a particular animal was possible in 21 of the 22 cases in which complete tests of drug-susceptibility were made.

It was considered that the chance of cross-infection between the animals was small, and it was concluded that the amount of air-borne infection in spaces occupied by persons with pulmonary tuberculosis, though small, is enough to account for the spread of the disease.

H. G. Calwell

EDWARDS, Phyllis Q. & EDWARDS, Lydia B. **Story of the Tuberculin Test from an Epidemiologic Viewpoint.** *Amer. Rev. Respiratory Dis.* 1960, Jan., v. 81, No. 1, Pt. 2, pp. iii + 47, 18 figs. [93 refs.]

This paper brings together a great deal of knowledge and speculation about tuberculin sensitivity much of which has already been presented in papers already reviewed in the *Bulletin* [1960, v. 35, 136, 365].

Doubts about the specificity of the tuberculin test in human beings arose in the United States in the 1930's when pulmonary calcification (hitherto regarded as a sure sign of tuberculous infection) was found in non-reactors. Faith in the test was restored when it was found that such calcification can also be caused by histoplasmosis, an infection which was prevalent in many of the areas in which non-reactors with pulmonary calcification were found. Coccidiomycosis is also a cause of pulmonary calcification in man.

Doubts in the other direction arose when it was found that a proportion of reactor cattle displayed no evidence of tuberculosis when examined after slaughter. Experimental work has shown that animals can be sensitized to tuberculin by a variety of acid-fast saprophytes and other mycobacteria. It has also been found that reaction to heterologous antigens tend to be less marked and more variable than those to homologous antigens. Non-specific reactions can therefore be distinguished with a fair degree of accuracy by comparative testing with various tuberculins.

The results of testing large groups of people in the United States and elsewhere were such that suspicion was aroused that in some areas most of the strong-dose tuberculin sensitivity was not caused by tuberculous infection and later suspicion was also being cast on small reactions to the 5 TU test. Comparative testing (as in cattle) revealed sensitivity to organisms other than the mycobacteria which cause tuberculosis in man, such as photochromogenic mycobacteria, the yellow bacillus, the Battey bacillus and others. Continuation of this work will probably lead to the discovery of the means by which true tuberculous infection can be accurately identified.

H. G. Calwell

ZITRIN, Charlotte M. **The C-Reactive Protein in Childhood Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1960, Feb., v. 81, No. 2, 266–70. [Refs. in footnotes.]

"In a group of 82 children with primary tuberculosis or its complications, the C-reactive protein was found to be positive in 24 of 50 patients with early, active disease, negative in 24 of 25 treated children who had been in the hospital more than two months, and negative in 6 of 7 patients with inactive disease (the positive test occurring in a child with healed tuberculous meningitis). The gamma globulin was abnormal more often than the C-reactive protein test. There was good correlation, however, between the latter and the alpha-2 globulin. Although a negative test does not preclude activity, a positive test is good evidence for the presence of active disease and is most helpful in equivocal cases as confirming evidence of active tuberculosis. When the C-reactive protein is positive early in the disease, conversion to negative with serial determinations appears to be a good prognostic sign."

PARLETT, R. C. & REHR, Carolyn A. **Further Studies on Gel Diffusion Tests in Tuberculosis. I. Methods for Standardization of the Antigen and Detection of Small Amounts of Antibody.** *Amer. Rev. Respiratory Dis.* 1959, Dec., v. 80, No. 6, 886–94, 3 figs. [14 refs.]

One of the purposes of this report was to describe a technique which will increase the sensitivity of the tube diffusion method described earlier [this *Bulletin*, 1960, v. 35, 38]. In this method a 10 cm. × 3 mm. tube was filled to a height of 3 cm. with a mixture of equal parts of antigen and 2% agar, and above this column was placed 1% agar to a depth of 0·75 cm. The tube was then filled with undiluted serum so that its antibodies could diffuse into the plain agar to produce precipitin bands by union with the antigens diffusing from the lower mixture.

The paper also describes experiments designed to test the validity of the method used for scoring the positive reactions; the positive sera of the previous study produced up to 6 bands of precipitate, and these were accorded a 1 + to 4 + score depending on the number of bands produced. That this method of scoring did in fact reflect the concentration of antibodies present in the serum, was shown by a standard anti-tuberculous rabbit serum producing 6 bands when diluted 1:4 and progressively decreasing numbers as the dilutions were increased to 1:64.

The technique for increasing the sensitivity of the test consists of replacing the test serum each day of the 7-day-observation period. Experiments with this modification were first done with dilutions of the standard rabbit serum and these showed that the number of bands increased progressively as the frequency of the replacements rose. The method was then tried on 21 samples of pooled human serum, and of the 11 pools which were negative by the original method, only 1 was negative by the modified method, 2 of the others gave a 1 + reaction, 4 a 2 + reaction, and 4 gave a 3 + reaction; the other 10 samples, which

gave only 1 + results by the original technique, gave 2 or 3 + reactions by the replacement method. These experiments also showed that increasing the length of the centre of column of agar to 2 cm. decreased the sensitivity of the test, and that similar results were obtainable with H37Ra and H37Rv antigens.

The authors also showed that when the antiserum is incorporated into the agar at the bottom of the tube and dilutions of the antigen are placed on top of the plain agar the precipitating potency of different samples of antigens can be compared. This claim was based on the observations that excess antigen inhibits maximal reaction, the day of maximal reaction varies with the antigen concentration, and with excess antigen the number of bands will decrease after the day of maximal reaction.

For routine examination of tuberculous sera the authors recommend that the tubes be inspected each day and the serum be replaced in those that are negative. An explanation of the dynamics of the test is given in the discussion. *S. R. M. Bushby*

MACKINNON, J. **Tuberculosis occurring during Steroid Therapy.** *Brit. Med. J.* 1959, Dec. 19, 1375–8, 1 fig. [26 refs.]

The appearance of tuberculosis during steroid therapy is well known [this *Bulletin*, 1956, v. 31, 903]. This paper describes 3 cases with some interesting features. In the first patient, who was being treated for cardiac failure and chronic discoid lupus erythematosus with systemic involvement, the X-ray of the chest on May 28th was normal and a further X-ray on August 31st was also normal. On September 3rd the patient developed low-grade pyrexia with a rising pulse rate, and died on September 28th, 1956. At the post-mortem examination, foci of caseous necrosis was found in many organs, spleen, lungs, kidneys, liver and lymph nodes. Sections stained for tubercle bacilli showed abundant organisms in the lymph nodes but somewhat fewer in the miliary lesions. The second patient was thought to have pulmonary sarcoidosis. Steroid treatment was started on April 30th, 1956. This was continued until May 1957 when she had a small haemoptysis. Both in April 1956 and May 1957 the X-ray appearance had remained unchanged, but in January 1958 the X-ray showed fresh infiltration at both apices and an irregular cavity with surrounding collapse behind the first rib. The sputum contained large numbers of tubercle bacilli. The patient recovered on antituberculous treatment.

The third patient, a female aged 61, was being treated for hypopituitarism. She was not seen for a period of 7 years, and when she returned she appeared to be hypothyroid again. The X-ray in May 1958 showed a normal chest. She was treated with thyroid and cortisone and on the 27th November was found to be drowsy and slightly disorientated. X-ray of the chest showed soft, bilateral apical tuberculous opacity with a miliary spread, and under anti-tuberculous treatment the condition cleared up, and the radiological appearance of the lungs improved. The author calls attention to the fact that the diagnosis of tuberculosis may be rendered difficult by the absence of fever, normal sedimentation rate, and lack of loss of weight.

As 2 out of these 3 patients had a normal chest X-ray at the start of steroid therapy he considers that it is wise to have regular chest X-ray during the course of such therapy. The possibility of the development of tuberculosis must always be kept in mind.

F. H. Young

FLEISHMAN, S. J. **The Aetiology and Treatment of Pleural Effusions in African Mine Labourers.** *Proc. Mine Med. Officers' Ass.* Johannesburg, 1959, July–Sept., v. 39, No. 370, 48–52. [24 refs. Discussion 52–5.

Pleural effusions are very common among the African mine labourers in the gold mining industry. The true incidence cannot be stated with accuracy because they appear to be classified in medical reports under a variety of diagnoses. The author premises that the majority of these cases are likely to have a common cause, be it infective, nutritional, neoplastic, or traumatic, embolic or allergic. These causes are briefly discussed and it is concluded that carcinoma of the lung, scurvy, pulmonary emboli or pneumonia are unlikely causes. Idiopathic pleural effusions are usually accepted elsewhere in the world as tuberculous; the reasons for this are given.

In this investigation, thorascopic examination was made of 71 unselected cases of pleural effusion; 31% showed the presence of tuberculosis either by histological, biological or cultural examination of biopsy specimens obtained from the pleura. In 4 others evidence of tuberculosis was obtained from culture of the pleural fluid etc., making 35% of cases in which the diagnosis of tuberculosis was established. Comparison of various methods of treatment was made, but no figures are given. 1 gm. of streptomycin sulphate intramuscularly was given daily for 8 weeks, together with 200 mgm. of isoniazid 3 times daily for 8 weeks with the addition of 10 mgm. of prednisolone 3 times daily for 2 days, followed by 5 mgm. daily for the rest of the 8 weeks. This method of treatment gave far better results than any of the others tried, and made this form of treatment the one of choice.

In the discussion which followed, very little in the way of evidence was produced against the hypothesis that these pleural effusions were due to tuberculosis. Dr. Linton said that he had seen hundreds of cases with effusion, but not one returned with tuberculosis of the lung, but this was not the general experience. The real trouble in accepting tuberculosis as the aetiology of pleural effusion appear to be the state of the law. If a case was diagnosed as tuberculosis compensation was given, but the worker was not allowed to return to the mines in any capacity. Many speakers felt that this would cause very great hardship.

F. H. Young

FLEISHMAN, S. J., COETZEE, A. M., MINDEL, S., BERJAK, J. & LICHTER, A. I., with the assistance of J. E. KERRICH. **Antituberculous Therapy combined with Adrenal Steroids in the Treatment of Pleural Effusions. A Controlled Therapeutic Trial.** *Lancet.* 1960, Jan. 23, 199–201. [12 refs.]

This paper reports various types of treatment and their results on all cases of pleural effusion which

occurred from June 1st, 1957 to September 26th, 1958, among the African labourers employed by one group of mining companies in South Africa. It was assumed, and evidence leading to this assumption is given, that pleural effusion without any other obvious cause was due to tuberculosis.

The patients were treated for a period of 8 weeks, and at the end of that time 73 patients were available for analysis. 4 methods of treatment were tried. The patients were allotted to the various methods of treatment in a random fashion which appears to have been satisfactory.

Treatment V:—was 500 mgm. of ascorbic acid intramuscularly daily for the first 14 days only.

Treatment P:—300,000 units of procaine penicillin intramuscularly twice daily for the first 14 days only.

Treatment T:—1 gm. of streptomycin sulphate intramuscularly daily for 8 weeks. 200 mgm. of isoniazid 3 times daily for 8 weeks.

Treatment TS:—The same as treatment T, with the addition of 10 mgm. prednisolone 3 times daily for 2 days followed by 5 mgm. 3 times daily for the remainder of the 8 weeks.

In other respects the patients' treatment was exactly the same.

A highly significant improvement took place at the end of 4 weeks in group TS compared with the groups V, T and P; although no further significant improvement took place in this group during a subsequent 4 weeks of treatment. The lack of improvement in the second 4 weeks can be explained on the grounds that after the initial beneficial effect there was little room for further improvement in most cases.

The clinical response to treatment T was noticeably superior to that of treatments V and P. Of the 53 patients treated by the methods V, P and T aggregated, in 8 the effusion had entirely resolved at the end of 8 weeks whereas of the 20 patients treated by method TS 12 showed complete resolution, giving a total result of 60% of the patients showing complete resolution on treatment TS against 15% on the other 3 treatments combined. *F. H. Young*

GEDDES, J. E. **Tuberculosis To-Day.** *Pub. Health.* 1959, Dec., v. 74, No. 3, 96–111, 2 graphs.

Geddes made a great reputation when he was in charge of the anti-tuberculous services in the city of Birmingham, but most of his friends and acquaintances thought he had undertaken a very big job when he went to look after those in Glasgow. Since he went there Glasgow anti-tuberculous services have been revolutionized. The present article represents his views on the treatment of tuberculosis, both curative and preventive; the article sets down in an attractive way what may be regarded as a standard résumé on the subject.

Geddes considers that rehabilitation is in danger of being neglected. In Glasgow the number of patients among the unskilled labouring classes was high, and the work on which these patients are normally engaged is frequently not suitable for them after their recovery from tuberculosis. He advocates the introduction of BCG vaccination at 10 years in school children.

He also thinks that consideration should be given to the adoption of chemoprophylaxis in all significant tuberculin reactors under 25 years, but in Glasgow one of the greatest difficulties is the lack of co-operation from many of the older patients of the lower social classes. Many of these, even if they allow themselves to be admitted to hospital, have to be prematurely discharged because of ill behaviour, or depart when the gentle conditions of life in hospital become oppressive. He ends: "How is this problem to be solved? Compulsion is an unattractive philosophy. Is there any other answer?" *F. H. Young*

SALIBA, A. **Tuberculosis Today: Some of the World Problems and Present Trends in Management.** *Brit. J. Dis. Chest.* 1960, Jan., v. 54, No. 1, 22–30. [35 refs.]

Saliba, writing from the United States of America, eschews complacency about the treatment of tuberculosis. Failures amount to 10–30% and provide a continuing reservoir of infection.

The main cause of many failures is inadequate initial treatment and many of these could have been avoided by high dosage of streptomycin and isoniazid daily rather than daily isoniazid and PAS or daily isoniazid with intermittent streptomycin.

Recent advances in treatment have called for increased laboratory services for the study of drug sensitivity and the determination of drug levels in serum. Many patients receive inadequate dosage of isoniazid because they are rapid inactivators of the drug and only subtherapeutic levels are reached in their serum.

Drug resistance may be inherent in some tubercle bacilli without mutation to resistance having occurred. The need for multiple drug regimens is therefore paramount. Chemotherapy can be so successful in sterilizing lesions that the presence of residual lesions in "open negative" cases is no longer necessarily an indication for operative surgical treatment.

The decline in mortality rates, already in progress before the advent of chemotherapy, has become swifter but this favourable trend is not universal. For example, there are 500,000 deaths from tuberculosis yearly in India, and there are some 2½ million persons with active tuberculosis for whom there are only 16,287 hospital beds. Other tropical countries present similarly unfavourable pictures.

In the underdeveloped countries of the world domiciliary treatment, single drug therapy and BCG vaccination play a major role in the control of tuberculosis but although the immediate results of treatment are good relapse and the emergence of drug-resistant strains of the tubercle bacillus may herald a black future. Tables list the morbidity and mortality and bed capacity for some 25 countries. *H. G. Calwell*

POOLE, G. & STRADLING, P. **Chemotherapeutic Pitfalls in the Treatment of Tuberculosis.** *Brit. Med. J.* 1960, Jan. 16, 161–5, 4 figs. [32 refs.]

It is generally accepted that anti-tuberculous drugs employed singly in adequate dosages lead to resistance

when given for any length of time; and that certain dual drug dosage schedules are fully acceptable as regards both efficacy and avoidance of resistance provided the organisms are fully sensitive before the start of treatment. If this treatment is given for a sufficient period up to 100% of sputum conversions can be expected. Unfortunately antimicrobial treatment as at present administered does not always produce this desirable result. This paper tries to elucidate the problem.

The records of 51 patients with resistance to one or more drugs were carefully examined together with full clinical records held at the Hammersmith Chest Clinic. In 32 patients sufficiently full clinical reports were available and the patients were still under the care of the clinic; the remaining 19 had been transferred elsewhere and were not available. A strict criterion of drug resistance was demanded.

18 patients had initial resistance to streptomycin, 26 to isonazid, and 3 to PAS; in addition 12 patients subsequently developed resistance. Out of 47 patients with initial resistance 14 were thought to have developed resistance owing to faulty prescriptions; these included the use of 1 drug alone, intermittent streptomycin B-PAS, and dipasic. In the remainder the authors satisfied themselves that the development of resistance was due to the failure to take adequate PAS. These types of failure are fully discussed.

The fate of the 32 patients is detailed: they consisted of 5 slight, 14 moderate, and 13 advanced cases; only 8 had quiescent disease; of the remaining 24, 9 still had active disease, and 15 had died of their disease. [These results are rather surprising as even in the pre-anti-microbial era they would have been considered very poor.] Carefully matched series of controls were obtained from records of the clinic and matched up against the patients considered here. In a carefully matched series only 2 of the patients have died; in neither case was death due to tuberculosis; the remaining 30 are alive and well.

The authors consider that the risk of getting resistant organisms is so great that, at any rate during the first 6 months of treatment, PAS combinations should not be used unless they can be given under strict supervision. They consider that the initial regime should be streptomycin, 1 gm. every day, with adequate isoniazid.

This paper deals with the problem which is likely to come increasingly to the fore in the next few years. The irregular discharge rate was 11% on the combined therapy and also on the isoniazid alone. At 5–8 months it was lower on the isoniazid alone (5%) than it was on the combination (11%).

[This appears to have been a very well conducted trial and the results may be taken as authoritative.]

F. H. Young

LEVY, D., HAAPANEN, J., RUSSELL, W. F., Jr. & MIDDLEBROOK, G. **Effect of Pyridoxine on Concentrations of Active Isoniazid in Serum.** *Amer. Rev. Respiratory Dis.* 1960, Jan., v. 81, No. 1, 102–4. [Refs. in footnotes.]

"The results of this study clearly demonstrated that the dosage of pyridoxine usually employed in clinical practice did not influence the six-hour serum concentration of that moiety of isoniazid that has a therapeutic action. The results were the same after a short course or after a prolonged course of therapy with both drugs."

KRAMER, W. **Cerebral Complication following Isoniazid Administration.** *Acta Tuberculosea Scandinavica.* 1960, v. 38, No. 1, 51–7, 1 fig. [20 refs.]

"A 16 year old patient was treated with PAS and INH, because of erythema nodosum with a slight tuberculous affection of both lungs. A daily administration of 12 gr PAS and 300 mg INH for 11 weeks was followed by acute signs of cerebral disease. After an initial stage of severe headache, vomiting, and blurred vision, a status epilepticus developed, followed by postparoxysmal dextral hemiparesis. The patient remained unconscious until the fourth day. Within a few days after the onset of the cerebral symptoms she was perfectly normal, the only traces being E.E.G. abnormalities which were still present six weeks later. This syndrome was thought to be caused by isoniazid intoxication of the brain. Cerebral complications resulting from this medication, its pathophysiology and prevention are discussed."

WOLINSKY, E. & KAPUR, V. N. **Evaluation of Cycloserine with High Dosage of Isoniazid in Chronic Treatment-Failure Pulmonary Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1959, Aug., v. 80, No. 2, 269–73.

This paper reports a further effort to evolve a regime to deal with failures in treatment. 35 patients, of an original 45, were treated for 9–13 months or until death, and divided into 3 groups. All were advanced and suitable for surgery. 11 patients were treated with cycloserine alone, 250 mgm. twice daily; 12 were treated with the same dosage of cycloserine plus isoniazid, 15 mgm. twice daily; and 12 received the same dose of cycloserine with isoniazid, 500 mgm. and 100 mgm. pyridoxine twice daily.

Toxic effects were noted in group 3 only, and 3 had to have treatment discontinued. Although temporary improvement in a few patients was noted, no definite permanent results were obtained; more patients died in the group treated with cycloserine only. Increasing cycloserine resistance appeared in 38% of patients. It was not possible to correlate lack of improvement with increased cycloserine resistance. The results reported do not seem to call for more extensive trial.

F. H. Young

SCHWARTZ, W. S. **VIII. Kanamycin in the Treatment of Pulmonary Tuberculosis, including Studies of Drug Toxicity.** (A Report of the Cooperative Study by Veterans Administration Hospitals.) *Amer. Rev. Respiratory Dis.* 1960, Jan., v. 81, No. 1, 105–7.

Kanamycin has been found to be active against tubercle bacilli which had become resistant to many

of the common antituberculous drugs. These included PAS, cycloserine, streptovaricin, streptomycin and isoniazid. Strains of tubercle bacilli resistant to neomycin and viomycin were not inhibited by kanamycin, although kanamycin-resistant strains were inhibited by viomycin.

This paper reports a small study of the toxicity and the therapeutic effectiveness of kanamycin by the U.S. Veterans Administration—Armed Forces.

In the first study 28 patients received kanamycin alone, 1 gm. daily intramuscularly, and 27 the same dose of kanamycin with tetracycline phosphate complex, 4 gm. daily. In the second study 11 patients received kanamycin alone, and 9 received the same dose of kanamycin, and PAS 12 gm. daily. It was intended to maintain these regimes for 6 months unless interruption or termination was required by unfavourable progress or toxic manifestations.

The patients selected were tuberculous with cavitated pulmonary disease with tubercle bacilli in the sputum, whose treatment had been unsuccessful on other chemotherapeutic regimes. Treatment had to be stopped prematurely for a variety of reasons in 65 of the 75 patients. Deafness occurred in 39% of those beginning treatment. Only 4 patients complained of vertigo. The proportion of patients becoming deaf was the same under all the regimes. Gastrointestinal disturbance from this drug made cessation of treatment necessary in 3 cases. In 2 cases treatment had to be stopped owing to renal toxicity after 2 months, although the finding of casts in the urine occurred very commonly.

The therapeutic effect was very poor. The sputum conversion rate under all regimes by culture was almost non-existent. The data available were much too small for any definite conclusions concerning the role of PAS or tetracycline phosphate complex in delaying the appearance of kanamycin-resistant tubercle bacilli. The authors conclude that in the absence of any considerable therapeutic benefit the risks of toxic deafness are far too large to allow the use of this drug in the doses tried in the investigation. *F. H. Young*

GERLACH, E. H., SCHERAGO, M. & HALL, H. E. **The Effect of Chemotherapy on the Tuberculin Sensitivity of Leukocytes from Tuberculous Patients.** *Amer. Rev. Respiratory Dis.* 1960, Jan., v. 81, No. 1, 100–101.

"The *in vitro* leukocytic sensitivity to tuberculin of 8 patients with active pulmonary tuberculosis was determined at six-week intervals before and during chemotherapy.

"The leukocytic sensitivity of 4 of the patients had decreased significantly within thirty-six and forty-two weeks before leaving the hospital; that of a fifth patient had decreased markedly at the end of sixty weeks; and that of the 3 remaining patients, to a nonspecific tuberculin sensitivity.

"The mean cytotoxic indices for the group showed a progressive decrease in leukocytic sensitivity from admission to the termination of the experiment. The skin test reactions to PPD of all 8 patients remained positive throughout the study period."

DRAPISCH, H. **Rehabilitating the Tuberculous in Israel.** *Amer. Rev. Respiratory Dis.* 1960, Jan., v. 81, No. 1, 9–16. [14 refs.]

About 735,000 immigrants reached Israel between 1949 and 1952. Of these 7,530 were found to have active tuberculosis. Most of these had serious emotional disturbances, had undergone severe physical suffering, and many were illiterate, having only had minimal education and no skills. At the Rehabilitation Centre for tuberculous patients between 1951 and 1957 68% were men. Details are given of the type of tuberculosis, extent of disease, and treatment received.

On leaving the Centre 86% were able to work 7 hours a day. Vocational training was very satisfactory, and on the whole, the graduates of the Centre achieved higher marks than did the graduates of other schools. When this vocational treatment was completed the emotional reactions usually became more pronounced when the patients were ready to leave the Centre. An important factor in mitigating this was the provision of suitable housing accommodation: this was achieved for 68% of the trainees.

88% of those leaving the Centre were placed in skilled jobs, 7% placed in jobs outside their trade, and only 5% could not be placed at all.

Follow-up observations which ran for more than 6 years showed that 80% of the patients succeeded in becoming absorbed into their communities as normal healthy citizens. *F. H. Young*

GORDON, C. G. I. & SHELLEY, J. H. **The Use of BCG Vaccine in Mantoux-Positive and Mantoux-Negative Persons in East Africa.** *Tubercle.* 1959, Dec., v. 40, No. 6, 425–31, 2 figs.

1,750 schoolchildren aged 5–16 years in a rural area of Tanganyika Territory were vaccinated intradermally with freeze dried BCG (0·1 mgm.) whether they were tuberculin reactors or not.

The preliminary test used was the Mantoux with 10 TU of OT. Reactions were read at 72 hours and vaccination was done 4 days later. 1,610 children were non-reactors (induration 0–4 mm.), and 140 (7%) were reactors (induration 5 mm. and over).

Accelerated reaction to vaccination (Koch phenomenon) was seen at 72 hours in 352 children of whom 223 were children who had been classified as non-reactors [and were not].

The largest Koch reactions were seen in children with the greatest degree of pre-vaccinal tuberculin sensitivity but it was also found that a child with a preliminary Mantoux reaction of 15 mm. could have a Koch reaction of 20–24 mm. or none at all.

Of the whole group of 1,750 children 53% had no visible vaccination lesion at 7 weeks; there were ulcers at the site in 10%, local abscesses in 3%, enlarged lymph nodes in 5% and scarring or skin nodules in 30%.

In the group of 352 with Koch reactions there was no visible reaction in 20% at 7 weeks, ulceration persisted in 20%, local abscesses in 6%, enlarged nodes in 10% and scars or skin nodules in 49%. All these

are reported to have healed without further trouble. [It is not stated how long they took to heal.]

One case of tuberculous cervical adenitis was seen 5 months after vaccination, and another child developed hilar adenitis which was presumed to be tuberculous. Both were strong reactors on admission to hospital; they had been non-reactors when tested originally and neither had shown the Koch reaction.

The conversion rate among the whole group was 80% at 7 weeks (92% in those over 10 years), and the authors therefore cast doubt on the potency of the vaccine. They speculate that with a more potent vaccine a higher proportion of troublesome reactions might occur than in the present series.

[This was a pilot survey to find out if it would be safe to vaccinate some 65,000 African schoolchildren without preliminary tuberculin testing. The authors do not state their conclusion.] *H. G. Calwell*

WEISS, D. W. **Vaccination against Tuberculosis with Nonliving Vaccines. I. The Problem and its Historical Background.** *Amer. Rev. Respiratory Dis.* 1959, Sept., Oct. & Nov., v. 80, Nos. 3, 4 & 5, 340–58; 495–509; 676–88. [263 refs.]

The bibliography appended to this review contains over 260 references to papers published between 1889 and 1958 in English, French, German and Italian. It excludes publications in Scandinavian, Slavonic and Oriental languages.

Koch had already demonstrated the efficacy of a non-living vaccine against tuberculosis as early as 1897 but many later writers have referred to his experiments as failures. Weiss thinks that this is probably because too much was asked of the vaccine.

From that early time to the present much work has been done on the immunogenic properties of killed mycobacteria but the development of dead vaccines has been almost eclipsed by the discovery of the "vaccinating abilities of BCG".

The various non-living vaccines discussed in th course of the review are tabulated according to the method of preparation. The largest number of refe ences is to killing by heat. Other methods of prepara tion are killing by exposure to sunlight or ultraviole irradiation, by formol, phenol, urea or other chemica agents or physical means. Tubercle bacilli permitted t die spontaneously in various environments or foun dead after exposure to serum or organ emulsions hav also been used for preparing vaccines. Finally, cultur filtrates and extracts and fractions of tubercle bacil have also been used.

Perusal of the literature supports the conclusion c the majority that non-living vaccines possess about a much immunizing power as living vaccines prepare from attenuated tubercle bacilli.

Weiss discusses at some length the question why non living vaccines have so often and so decisively bee condemned as ineffective. The success of the first c all vaccines, living vaccinia virus, had created a bia in favour of a living vaccine which was not soon o easily dispelled. Another reason for the disparagemen of the non-living vaccine compared with the living vac cine was that while even a very small number of livin bacilli may eventually synthesize enough protectiv material to afford some degree of immunity even 100-fold amount of dead vaccine may be insufficien to do so. On the other hand the administration o too large a dose of dead vaccine at one time ma cause severe toxic reactions and so nullify an immunizing effect. Other cogent reasons for the lac of development of non-living vaccines against tuber culosis are given and discussed.

Weiss mentions that a reinvestigation of th immunizing power of non-living vaccines, with statisti cally significant numbers of animals and with widel varied experimental conditions of vaccination, wa begun in 1952. Results will be published later.

H. G. Calwell

VENEREAL DISEASES

FIUMARA, N. J. & WHITE, H. **Primary Syphilis in an Eighty-One-Year-Old Man.** *New England J. of Med.* 1960, Jan. 7, v. 262, No. 1, 31.

"An eighty-one-year-old man presenting himself with a penile lesion was found to have primary syphilis. When interviewed for contacts, he admitted sexual exposure with 4 different women during a period of approximately three months. It is not our intention to initiate an international contest among physicians over who has had the oldest patient with primary syphilis, but we want to emphasize two important lessons to be drawn from this case—namely, that any genital lesion should be suspected of being syphilis until proved otherwise and that syphilis is no respecter of age."

STEEL, R. **G.P.I. in an Observation Ward.** *Lancet.* 1960, Jan. 16, 121–3.

12 cases of untreated and 2 of recently treated GPI are described; their ages varied from 27 to 72 and all but 2 were males. The clinical picture varied a great deal and in several the clinical signs were fa from typical; however, all 12 had increase of cells and protein and positive WR in the cerebrospinal fluid [CSF] with typical Lange curves; all had positive blood WR and Kahn except 1 who had a negative blood WR. None gave a history of syphilis.

Of the 2 treated patients, in 1 no pathological find ings are given but the diagnosis was "in no doubt" the other had a history of syphilis 11 years previously his CSF was typical of GPI [except that apparently no WR of the CSF was done] and his blood WR wa negative but Kahn positive; the only treatment recorded was 1 injection of penicillin before readmission to the observation ward.

GPI is well known to present very variable signs and symptoms and this is well illustrated in this series whether "neurosyphilis is probably more common than is assumed" depends on who makes the assumption probably not venereologists. *T. E. Osmond*

BELL, R. E. **The Value of Routine Serologic Tests for Syphilis on Hospital Admission.** *Amer. J. Clin. Path.* 1959, Dec., v. 32, No. 6, 521–5.

13,372 specimens of serum from patients routinely admitted to a hospital in Alberta, Canada, were submitted to the Kahn presumptive test and if this was positive to the Kahn standard and Wassermann (WR) also. In 106 patients reactions were positive [though why a doubtful standard Kahn should be considered positive (as is stated in the text) is not clear]. The patients included 35 over 65 years of age, of whom 10 were known to be syphilitic, and 71 under 65 including 30 known syphilitics, 19 not followed up, 15 falsely positive and 7 newly discovered cases of syphilis. Only 2 of these 7 show much of interest; 1 suffered from anaemia and bleeding haemorrhoids, had a negative Kahn and positive WR and was "probably a true example of syphilis" and 1 had a positive Kahn and negative WR without evidence of active disease but regarded as a "true positive"; [the diagnosis in these 2 cases seems to be founded on somewhat tenuous evidence]. It is generally found that the incidence of positive reactions in routine hospital admissions lies between 0·7 and 2·6%; in this report it was 1·06%. The cost is estimated to be about half a dollar per test and the cost of discovering a single case subsequently successfully treated approximately 1,600 dollars.

The pros and cons of routine STS are discussed and the author thinks they are worth while except in children and persons over 60 years of age.

T. E. Osmond

GUPTA, S. P., GUPTA, N. P. & AGARWAL, D. S. **Some Observations on the Serological Tests for Syphilis.** *J. Indian Med. Ass.* 1959, Nov. 1, v. 33, No. 9, 351–4. [18 refs.]

These authors carried out large numbers of tests for syphilis using 2 or more of the following tests in parallel: Wassermann (WR with crude antigen), Kahn, Meinicke, VDRL and Wassermann with cardiolipin antigen (CWR). They calculated results as showing agreement, partial agreement and disagreement but in giving percentage results the first 2 were combined.

On 90,494 sera WR and Meinicke agreed in 87·8%; on 3,942 sera WR and Meinicke agreed in 91%, WR and VDRL in 90% and VDRL and Meinicke in 92%; on 772 sera WR and Kahn agreed in 92%, VDRL and Kahn in 86·4% and Kahn and Meinicke in 93·8%.

On 2,558 sera which showed discrepant results with WR and Meinicke, agreement between CWR and VDRL was 86·6%, between WR and CWR 88·3%, between WR and VDRL 74·5%, between CWR and Meinicke 76·2% and between VDRL and Meinicke 83·6%; of 385 sera from this series retested on fresh samples WR and Meinicke only agreed in 61·3%.

When repeat WR and Meinicke tests were carried out on 326 sera diagnosed clinically, discrepant results were found in 5 out of 10 primary syphilis, 32 out of 73 secondary syphilis, 20 out of 46 "skin lesions", 18 out of 49 "nervous disease" and 19 out of 53 "other chronic infections". [The fact that both tests were negative in 32 out of 72 cases of "secondary syphilis" suggests that either the clinicians or the tests were sadly at fault.] A somewhat incomplete and unrepresentative selection of other workers' results is appended.

According to these authors the WR gave most and Kahn fewest positive results while Meinicke and VDRL showed the closest agreement; there is no indication which is the most reliable test as far as specificity and sensitivity are concerned.

T. E. Osmond

PORTNOY, J. & GARSON, W. **A Preliminary Report on RPR Test for Syphilis using Unheated Serum.** *Pub. Health Rep.* Wash. 1959, Nov., v. 74, No. 11, 965–8.

These authors carried out the Rapid Plasma Reagin test (RPR) [this *Bulletin*, 1959, v. 34, 1245] on 2 series of specimens: (1) 149 specimens were subjected to the RPR with serum, RPR with plasma, VDRL and TPCF 50 (treponema pallidum complement-fixation test); (2) 1,740 specimens from a serological survey in North Carolina were tested by the RPR test with serum.

In group (1) RPR (serum) and VDRL were reactive in 45·0%, TPCF 50 in 47·0% and RPR (plasma) in 49·0%; RPR (serum) and RPR (plasma) agreed in 96·0% and RPR (serum), VDRL and TPCF 50 agreed in 93·3%.

In group (2) RPR (serum) gave 9·0% reactive, 2·8% weakly reactive and 88·3% non-reactive results; 417 of the 1,740 specimens were selected for testing by VDRL and TPCF 50 tests 6–7 days latter; results showed RPR (serum) reactive in 45·6%, VDRL in 49·9% and TPCF 50 in 54·5%; RPR (serum) agreed with VDRL in 86·8% and with TPCF 50 in 82·7%.

When RPR (serum) test was repeated on 68 specimens only a very slight loss of reactivity was noted.

It is concluded that the PRP test on unheated serum is a useful screening test though slightly less reactive than the plasma test; it compares favourably with the VDRL test.

T. E. Osmond

BORIES, S. & LAIGRET, J. Réactions sérologiques de réagine, de la syphilis et tréponématoses à Tahiti d'après deux enquêtes effectuées en 1958. [**Reagin Serological Reactions of Syphilis and the Treponematoses in Tahiti according to Two Enquiries in 1958**] *Méd. Trop.* Marseilles. 1959, Nov.–Dec., v. 19, No. 6, 670–82.

Struck and surprised by the statement that syphilis represented more than 50% of the morbidity in a part of Tahiti, these authors examined the sera of 2,370 French Polynesians residing in the island.

The first series comprised 1,334 subjects including babies under 1 year, children 2–6 years, blood donors, candidates for employment, rural workers and post-natal mothers. Reactions employed were Kahn standard and Kline, VDRL and Kolmer with cardiolipin antigen; the second series included 1,036 school children in Papeete aged 6–18 years and the reaction used was a micro-quantitative method carried out on dried blood similar to the Kline exclusion test. Percentages of

positive results were: up to 3 years 7, 3–5 years 8, 18–45 years 11, 6–10 years 5·12 and 11–18 years 4·91. Dissociated reactions among the 4 tests in series 1 are discussed but the authors do not think many "false" reactions occurred in spite of the presence of certain tropical diseases; they think the reactions in the newborn indicate congenital syphilis but clinical signs in these and in all other categories were largely conspicuous by their absence. Yaws no doubt accounted for some of the positive serum reactions but most were due to (latent) syphilis. It is stressed that positive reactions occurred much more frequently in some parts of the island than others. [It seems a pity that some confirmatory test such as the TPI was not available.]

T. E. Osmond

ALLINNE, M. & BERANGER, J. Étude comparative de differentes reactions serologiques de la syphilis. Reactions lipidiques et treponemiques. Test de Nelson. [**A Comparative Study of Different Serological Reactions in Syphilis; Lipoid and Treponemal Reactions; TPI Test**] *Algérie Méd.* 1959, Apr., v. 63, No. 4, 417–30. [33 refs.]

These authors tested some 1,200 sera from persons who were syphilitic or suffering from conditions suggestive of syphilis; the reactions employed were: TPI, Kolmer and Kline (with cardiolipin antigen), Kahn (with lipoid antigen) and the Reiter complement-fixation test (Pallignost).

In 892 cases there was agreement between TPI and the other tests (all positive in 271 and all negative in 621) and in 261 there was disagreement.

The 621 negative cases included 144 syphilitics, treated or untreated. There were 198 cases with TPI positive and other tests negative; in 145 cases of syphilis with TPI positive, Reiter test was positive in 121, Kline in 112, Kolmer in 81 and Kahn in 3; in 63 cases with TPI negative Reiter was positive in 22, Kline in 40, Kolmer in 25 and Kahn in 9; in 38 of these the patient was not syphilitic. In 47 cases with TPI doubtful Reiter was positive in 12, Kline in 14, Kolmer in 8 and Kahn in 5.

In a considerable number of cases quantitative tests were carried out. The following are the percentages of agreement with the TPI test of the other tests: sensitivity—Reiter 83·5, Kline 81·6, Kolmer 75 and Kahn 58·4; specificity—Reiter 98·4, Kline 94, Kolmer 96 and Kahn 98·2.

It is concluded that: the TPI test is the best of all, that the Reiter test is superior to cardiolipin tests, the Kahn test is the least sensitive and that quantitative tests are valuable in studying syphilitics under treatment.

Detailed results of the various tests with diagnoses are set out in 14 tables. *T. E. Osmond*

BRITISH CO-OP. CLIN. GROUP. **An Examination of the Treponemal Immobilization Test in the Investigation of Positive Serological Tests for Syphilis in Pregnancy. An Investigation.** *Brit. J. Venereal Dis.* 1959, Sept., v. 35, No. 3, 162–8, 1 fig. [10 refs.]

This group examined the results of TPI tests in pregnant women giving positive serum tests for syphilis (STS). A questionary was sent to 58 clinics and as a result 503 case reports (423 white and 80 coloured women) were available; valid TPI tests were carried out on 176 of the white and 43 of the coloured patients this test was reactive in 73·8% of the former and 88% of the latter.

31 of the 130 TPI positive and 3 of the 46 TPI negative white patients showed clinical evidence of syphilis; the corresponding figures for coloured women were 2 out of 38 and 1 out of 5.

There was family evidence of syphilis in 23 of the TPI positive and 2 of the TPI negative white cases. The outcome of pregnancy showed very little real evidence of congenital syphilis in the children.

In general the TPI results agreed fairly closely with the clinical diagnoses and TPI and STS agreed much more closely when the latter agreed among themselves than when they disagreed.

Thus negative TPI reactions may be expected in about 23% of sero-positive pregnant women but in a very rare case the TPI may be negative in the presence of syphilis. *T. E. Osmond*

SEQUEIRA, P. J. L. **An Examination of the Treponemal Wassermann Reaction and Reiter Protein Complement-Fixation Test.** *Brit. J. Venereal Dis.* 1959, Sept., v. 35, No. 3, 139–47, 1 fig. [33 refs.] Discussion 147–8.

This is a highly technical and complicated article so that only the main conclusions can be given in an abstract.

After discussing the various serum tests for syphilis and giving some account of their history the author points out that treponemata have 3 essential antigens, *i.e.* lipoid, thermolabile and thermostable; all 3 are possessed by virulent and avirulent strains but the Reiter strain also possesses a fourth (organ-specific for brain, lipoid). The reactions considered are standard serum tests for syphilis (STS), treponemal immobilization test (TPI), treponemal immune adherence test (TPIA), treponemal agglutination test (TPA), treponemal complement-fixation test (TPCF), treponemal Wassermann reaction (TWR), Reiter complement-fixation test (RCF) and Reiter protein complement-fixation test (RPCF); of these only TWR, RCF and RPCF are suitable for routine work. In addition the standard WR, WR with cardiolipin, Price's precipitation and Kahn tests were carried out on a number of sera from a VD clinic, general hospital cases, blood donors and selected "problem" cases.

Results are set out in 10 tables, comparisons are made and the results discussed; particular attention is paid to a comparison between TWR, RPCF and TPI with especial reference to clinical findings. The author recommends for diagnosis the RPCF and 2 tests for reagin, with TPI for confirmation; a reagin test plus RPCF should have a specificity of 99·99%; if they disagree a TPI test should be done; this will rule out biologically false positive reactions. *T. E. Osmond*

DUNLOP, E. M. C. & PRICE, I. N. O. **Clinical Assessment of the Treponemal Wassermann Reaction.** *Brit. J. Venereal Dis.* 1959, Sept., v. 35, No. 3, 149–61, 8 figs.

These authors carried out this reaction (TWR) in parallel with the Wassermann reaction (WR) and Price's precipitation test (PPR) on 4,105 patients including 3,078 men (2,300 white and 778 coloured) and 1,027 women (875 white and 152 coloured); total TWR's were more than 10,000. Results are set out in 16 tables and 8 figures.

A control group included 647 persons; TWR was positive in 4·4% of whites and 41% of coloured persons with no history of antibiotic treatment but on the other hand out of the whole 4,105 patients 13 presumed non-syphilitic persons gave a positive TWR which was subsequently confirmed by TPI tests. As regards reproducibility in one series of 35 patients TWR was discordant on repeat in 10 and in another it was discordant in 3% of white and 26% of coloured persons.

The results in a group of 439 syphilitic persons are as follows: in sero-negative cases TWR gave far more positives than WR or PPR; in sero-positive primary syphilis TWR was positive in 36%, WR in 19%, PPR in 8% and TPI in none; in secondary syphilis after treatment TWR was positive in 40%, WR in 16% and PPR in 16%; in early latent cases the respective figures were 7 out of 11, 15 out of 30 and 14 out of 30, in latent syphilis 69%, 73% and 65%, in late syphilis 61%, 71% and 69% and in late congenital syphilis 74%, 82% and 84%.

In 103 coloured persons suffering from "syphilis or yaws" TWR was positive in 83%, WR in 76%, PPR in 67% and TPI in 100%.

In 24 non-treponemal reactors (TPI negative) TWR was positive in 15, WR in 13 and PPR in 5.

It is concluded that TWR shows poor specificity and reproducibility and cannot therefore replace TPI.

T. E. Osmond

LAIRD, S. M. **A Clinical Assessment of the Treponemal Wassermann Reaction.** *Brit. J. Venereal Dis.* 1959, Sept., v. 35, No. 3, 169–74, 1 fig.

The treponemal Wassermann reaction (TWR) was compared with TPI and also with a standard Wassermann (SWR) and Price's precipitation reaction (PPR) on sera from patients known to have had syphilis and from blood donors.

Detailed results are set out in 13 tables and 1 figure.

In a series of 120 patients with syphilis TPI remained positive much longer than the other 3 tests; in 35 cases where both TPI and TWR were carried out the former was negative in 4 (11%) and the latter in 18 (51%); the two tests agreed in 20 (62%) cases.

Of 103 blood donors investigated 23 had late congenital, 10 late acquired, and 45 latent syphilis, while 25 gave non-treponemal reactions; in 20 cases definitely syphilitic TPI was always positive but TWR was negative in 44%. Among 106 antenatal cases TPI and TWR were carried out in 18 cases; there was agreement in 69% but TWR was falsely positive in a high proportion.

In 46 "problem" cases these two tests agreed in only 11 of 16 cases. A considerable number of results with both TPI and TWR were "fluctuating" presumably owing to varying amounts of antibody. The author found TPI falsely negative in 11% of his cases (admittedly selected) [which is somewhat surprising] and concludes that TWR cannot replace TPI and is little superior to SWR and PPR. *T. E. Osmond*

WILKINSON, A. E. & JOHNSTON, N. A. **Results of Parallel Tests with the Reiter Protein Complement-Fixation Test, the Treponemal Immobilization Test, and the Treponemal Wassermann Reaction on 1,046 Sera.** *Brit. J. Venereal Dis.* 1959, Sept., v. 35, No. 3, 175–80. [31 refs.]

These authors carried out parallel tests on 149 presumed normal, 133 syphilitic, 827 "problem" sera and on 86 sera from patients with lepromatous leprosy; the tests employed included the Reiter protein complement-fixation (RPCFT), *Treponema pallidum* Wassermann (TWR), standard Wassermann (WR), Price's Precipitation (PPR) and *Treponema pallidum* immobilization (TPI) tests.

Of the 149 normal sera all were negative except 3 positive with TWR; of the 133 syphilitic sera TPI was positive or doubtful in 118, RPCFT in 98, TWR in 89, WR in 91 and PPR in 64; in 466 sera found positive on routine testing RPCFT agreed best with TPI particularly in the TPI-negative group where there were only 2 disagreements compared with 60–88 with the other tests; in 45 possible yaws cases TPI and RPCFT agreed closely; in 236 possibly syphilitic sera RPCFT again agreed most closely with TPI; in 86 leprosy sera RPCFT gave no positive reactions where TPI was negative but TWR gave a very high percentage of positive reactions.

It is concluded that RPCFT is more sensitive than TWR or the other reactions and agrees reasonably well with TPI; TWR as at present performed is unreliable.

T. E. Osmond

FOSTER, W. D., NICOL, C. S. & STONE, A. H. **Further Assessment of the Reiter Protein Complement-Fixation (RPCF) Test in a Routine Serological Laboratory.** *Brit. J. Venereal Dis.* 1959, Sept., v. 35, No. 3, 181–3.

The RPCF test was carried out in parallel with a standard Wassermann reaction (WR) and Price's precipitation reaction (PPR). All 3 tests were positive in 178 cases, WR or PPR or both were positive and RPCF negative in 13 cases, and WR and PPR negative and RPCF positive in 97 cases [this *Bulletin*, 1959, v. 34, 124]. Of the 13 cases 8 had a history of syphilis and 5 were possible biological false positives; of the 97 cases 82 had a history of syphilis or yaws and 15 were coloured patients who may have had yaws.

Over a period of 9 months there were 151 discrepancies between RPCF and PPR; of these 116 were positive with RPCF and TPI but negative with PPR, 4 were positive with PPR but negative with RPCF and

TPI, 2 were negative with RPCF and positive with the other 2 and 28 were positive with RPCF and negative with the other 2.

Of the 28 cases 8 had had a sore or a treponematosis, 8 had had urethritis and 18 had been treated previously with penicillin.

In general it was found that RPCF became positive before TPI and remained so for long after treatment.

In 140 blood donors 2 were RPCF positive and both were TPI positive. In 192 sera repeat RPCF tests showed no change in 155 but 37 gave variable results.

It is concluded that RPCF is technically simple, depends on antibody different from reagin and is sensitive, reproducible and appears to be specific.

T. E. Osmond

BÖTTCHER, Gisela & HIPPIUS, H. Immunbiologische Untersuchungen des Liquor cerebrospinalis und Diagnostik der Neurolues. (Zugleich ein Diskussionsbeitrag zu der Arbeit von H. G. Gram: "Die Spirochätenagglutination im Liquor".) [**Immunological Studies of Cerebro-Spinal Fluid and the Diagnosis of Neurosyphilis**] *Deut. med. Woch.* 1959, Aug. 28, v. 84, No. 35, 1557–9, 1584. [12 refs.]

In the laboratory diagnosis of neurosyphilis by the reaction of spirochaete agglutination of ROEMER and SCHLIPKOTEN [this *Bulletin*, 1953, v. 28, 622] in a large series of cases, 740, GRAM [*ibid.*, 1959, v. 34, 533] has described 96% of positives in neurosyphilis and only 1·8% of false positives in other conditions whereas the present authors in a series of 942 cases have observed only 34% of positives in neurosyphilis and 2·3% of false positives in other conditions.

The explanation of this marked discrepancy is found in the wider outlook of the authors in establishing the diagnosis of neurosyphilis. They take history, clinical condition, cell and chemical investigation of the cerebrospinal fluid and a wider range of laboratory procedures, including the treponema immobilization test, into account.

Gram has limited his positive neurosyphilis to those positive by one or more of the following reactions: Wassermann, second Meinicke precipitation, citochol, cardiolipin-microflocculation and spirochaete agglutination.

J. W. McLeod

KING, A. J. **Gonorrhoea and other Venereal Diseases.** *Brit. Med. J.* 1959, Dec. 19, 1396–8. [34 refs.]

Antibiotics have revolutionized the drug treatment of most venereal diseases, but resistance to these drugs seems to be developing. The dosage of penicillin for gonorrhoea should be 600,000 to 1,200,000 units (compared with 200,000 units a few years ago) or 1 gm. streptomycin; penicillin by mouth is effective (penicillin V 2–3 mega units over a few days) and is less likely to cause sensitivity reactions but should be reserved for intelligent and co-operative patients. Most of the broad spectrum antibiotics are also effective and may be used when penicillin is contra-indicated.

Chancroid usually reacts well to sulphathiazole or sulphadiazine; if these fail streptomycin, 1 gm. daily for 5 days, or one of the tetracyclines should be tried. aspiration of suppurating buboes and free drainage are very important.

Lymphogranuloma venereum should be treated initially with sulphadiazine 5 gm. daily for 5–7 days; if this fails tetracyclines or chloramphenicol intramuscularly should be tried.

Granuloma inguinale usually responds to antibiotics *e.g.* streptomycin 4 gm. in divided doses daily for 5 days or chloramphenicol, chlortetracycline, oxytetracycline or carbomycin; relapse is common and retreatment often necessary with the same or another drug.

Non-specific (abacterial) urethritis is difficult to cure a combination of a sulphonamide and streptomycin seems to give the best results; oxytetracycline and tetracycline are worth trying.

It is stressed that drugs constitute only one aspect of the treatment of venereal diseases and they should be used with discretion; a warning is given that the rapid subsidence of symptoms [or perhaps, better, signs] does not necessarily imply cure.

T. E. Osmond

LAIRD, S. M. & MORTON, R. S. **The Ecology and Control of Gonorrhoea.** *Brit. J. Venereal Dis.* 1959 Sept., v. 35, No. 3, 187–96. [33 refs.]

The incidence of gonorrhoea in any community at any one time is not and cannot be known but trends can be studied. The disease increased during and immediately after the last war, tended to decrease in the next few years but since 1951–52 has levelled off or increased slightly. Tables are given showing the number of *known* cases in various countries in 1948–57, in England and Wales from 1932–58 and in Manchester and the surrounding region. In turn these authors consider the effects of race, prostitution, alcohol, socio-economic factors, public education, the asymptomatic female carrier, contact tracing and the effect of treatment. There is a good deal of disagreement as to the effect of prosperity or economic depression on the incidence of the disease but most people are agreed that alcohol, unstable family life, immigration, asymptomatic female carriers and other reservoirs of infection favour the persistence of gonorrhoea and that the disease is one of large cities rather than the countryside. Effective treatment, good contact tracing, improved socio-economic conditions and implementation of the Street Offences Bill are on the credit side of the balance sheet but on the debit side must be placed diminished sensitivity to penicillin, the asymptomatic female carrier, infected immigrants and the spread of prostitution in public houses, clubs, dance-halls, etc.

Until some form of immunity can be achieved control of gonorrhoea is not likely to be attained; what is needed is biological research particularly into the gonococcus; other measures such as education, contact tracing, provision of treatment etc. will never eradicate the disease. [This is a well thought out and presented article which should be studied by all those interested in the subject.]

T. E. Osmond

OATES, J. K., WHITTINGTON, M. J. & WILKINSON, A. E. **A Note on the Results of Cultural and Serological Tests for Pleuropneumonia-Like Organisms in Reiter's Disease.** *Brit. J. Venereal Dis.* 1959, Sept., v. 35, No. 3, 184–6.

Cultural and complement-fixation tests (CFT) were carried out on 2 groups of patients in order to find out whether pleuropneumonia-like organisms (PPLO) were responsible for Reiter's disease: (a) those with the disease, (b) those with a past history of the disease. For the CFT 2 antigens were employed one from PPLO isolated from a case of non-gonococcal urethritis (NGU) and one from a case of Reiter's disease (R). 54 patients, 31 with active and 23 with inactive disease were investigated; of the 31, 9 gave positive and 17 negative cultures (5 were omitted), 16 had positive and 15 negative CFT; 5 were positive and 11 negative to both tests while 4 gave positive cultures and negative CFT and 11 the reverse. When the 2 antigens were compared in active cases both were positive in 10 and negative in 15. NGU was positive and R negative in 1 and the reverse in 5. Of the 23 inactive patients only 2 gave positive CFT and none gave positive culture.

These results suggest that PPLO may possibly play a part in the causation of Reiter's disease.

T. E. Osmond

KING, A. J. **Advances in the Treatment of Venereal Disease.** *Practitioner.* 1959, Oct., v. 183, No. 1096, 467–77. [36 refs.]

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and Other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

GIORN. DI MALATTIE INFETTIVE E PARASSIT. 1959, July, v. 11, No. 7, 469–690, numerous figs. [Numerous refs.] Società Internazionale per lo studio delle malattie infettive e parassitarie. Secondo Congresso Internazionale di Patologia Infettiva (Milano, 6–10 Maggio 1959). **[International Society for the Study of the Parasitic and Infectious Diseases. Second International Congress of Infective Diseases]**

The proceedings of the second International Congress of Infective Pathology held at Milan in May, 1959 are reported. These consist of 3 Symposia on (I) mechanisms of defence of the body against infective illness, (II) staphylococcal infections, and (III) blood culture. They are preceded by an extensive monograph on viral hepatitis by F. DE RITIS (pp. 469–524) and a shorter communication on bacterial hepatitis by K. TODOROVITCH (pp. 525–550).

The last is largely a summary of the pathological changes associated with infections localized in the liver or with the lesions which appear in the liver in the course of a septicaemic infection such as typhoid fever. A great deal of the ground covered is already familiar to pathologists.

De Ritis presents a comprehensive review of the literature of viral hepatitis which covers almost every aspect of this subject. Among these are the differentiation of epidemic and serum hepatitis viruses, the part played by viruses in the genesis of cirrhosis, alterations which may appear in electrocardiographic and encephalographic tracings in this disease, the methods of sterilizing plasma pools which may have been infected by a donor who was a latent carrier of virus, and many others.

In respect of diagnosis, special emphasis is given to the recognition of the unusual abundance of enzymes in the plasma which, presumably, have been liberated by the disintegrating liver cells.

The author claims that the findings which he and his colleagues have described have greater diagnostic significance than any other tests so far introduced and are particularly valuable in non-icteric cases. A very great increase in the transaminase content of the plasma is observed and the normal quantitative relationships of the transaminases acting on alanine and aspartic acid respectively in the presence of ketoglutaric acid are reversed. In the normal person the aspartic transaminase slightly exceeds the alanine transaminase so that the ratio of aspartic transaminase to alanine transaminase has a value of 1 or more, whereas in hepatitis the reverse holds, the values are considerably below 1 and this relationship persists even during recovery when there is a lesser total transaminase content. The excess of enzymes in the plasma is not restricted to the transaminases. Many other increases have been observed by de Ritis and his colleagues and by independent observers but it is claimed that the alteration in the transaminases described is more sharply related to virus hepatitis.

Yellow fever is not excluded by this test but there are many countries where viral hepatitis is encountered in which this difficulty does not arise.

Symposium I

The papers by H. ISLIKER (pp. 553–555) and by C. ZANUSSI and P. A. TASCHINI (pp. 561–574) deal with the amounts of properdin present in the tissue fluids in various conditions of disease and the methods of determining its presence. The many complexities of such observations are emphasized and doubt is expressed about their diagnostic and prognostic significance at the present time.

G. DE MURALT (pp. 578–579) draws attention to the slow development in the newborn of the globulins essential for immunity and points out the danger of a hypogammaglobulinaemia at this stage which may make the infant unduly susceptible to the administration of anatoxin or bacterial vaccine.

H. E. SCHULTZE (pp. 593–600) discusses the differentiation of proteins of the serum by the method of immunoelectrophoresis and the difficulty of distinguishing them from antibodies of nearly similar composition.

Symposium II

This series of papers deals mainly with subjects on which much work has been published of late.

J. M. SALA GINEBREDA (pp. 616–628) gives an account of pulmonary staphylococcal infection in infants as seen in Barcelona. In 44 cases he records a mortality of 25% but there were no deaths in 10 of these who had received surgical treatment. The importance of early surgical treatment in infantile staphylococcal infections is also emphasized by M. GROB of Zurich (pp. 629–632) on account of delay involved in selecting an antibiotic to which the strain in question is sensitive.

J. PROCHAZKA (pp. 658–660) contributes an interesting discussion of the control of obstinate staphylococcal infections by agencies other than antibiotics and cortisone. He mentions good results in checking infantile staphylococcal infections in maternity clinics by immunization of the mothers with anatoxin in the later stages of pregnancy.

Symposium III

R. FASQUELLE and D. CHRISTOL (pp. 663–673) insist on the frequent occurrence of bacteriaemia as opposed to septicaemia and claim that, because of frequent eruption of bacteria into the bloodstream and their brief sojourn there, a positive blood culture does not indicate the existence of septicaemia, which is only indicated by the clinical condition of the patient. They also suggest that the concept of septicaemia as a condition in which bacteria multiply in the blood is a misleading one mostly held by Anglo-Saxon writers. True as this may be in some aspects, it is less convincing when no mention is made of the importance of the technique of blood culture and of the many erroneous positive results which occur on account of an inadequate technique.

B. KASSUR (pp. 687–690), writing from Poland, however, seems to be on firmer ground when he gives a careful analysis of the period in which bacteriaemia may follow disruption of inflammatory foci, of the types of bacteria which appear in such circumstances and of the technical sources of error. He emphasizes the value of blood culture in recognizing the persistence of infection where the patient is under partial control by antibiotics. [It may well be that the actual growth of bacteria in the blood does not occur except as an agonal phenomenon and that persisting septicaemia as detected in the early days of typhoid fever is due to the persistent feeding of bacteria to the bloodstream from foci outside the circulation, but the finding of a positive blood culture of typhoid or paratyphoid bacilli by a reasonably competent bacteriologist is not surpassed as conclusive evidence by any other type of observation in clinical medicine.] *J. W. McLeod*

WILSON, R. J., MOSS, G. W. O., POTTER, F. C. & MACLEOD, D. R. E. **Diphtheria and Tetanus Toxoids combined with Pertussis and Poliomyelitis Vaccines. Clinical Trial of a Quadruple Antigen.** *Canadian Med. Ass. J.* 1959, Sept. 15, v. 81, No. 6, 450–53, 1 fig.

This paper describes a clinical trial of quadruple antigen (diphtheria, pertussis, tetanus and polio, *i.e.* DPT Polio) prepared by the Connaught Medical Research Laboratories in Toronto. This combined antigen was prepared in an effort to include prevention against poliomyelitis in the general scheme of prophylactic immunization in Canada. The poliovaccine was prepared with benzethonium chloride as preservative (not Merthiolate [thiomersal] and versene). The other components also contained benzethonium chloride and were specially concentrated and ultrafiltered. Each 1 ml. dose contained 0·92 ml. of standard poliovaccine, 40 Lf diphtheria toxoid, 8 Lf tetanus toxoid and 15,000 million *Haemophilus pertussis* organisms. The potency of the poliovaccine was slightly enhanced for monkeys in combination with DPT and appeared to be stable for up to 14 months at 4°C.

51 infants under 1 year old (12 were 3 months old and 27 others under 6 months, the remaining 12 being between 6 months and 1 year) were immunized with the combined vaccine and 8 with the poliovaccine alone; 3 doses were given at 4-weekly intervals. The first dose was 0·5 ml. for infants under 6 months and the remaining doses were of 1 ml. each. The response to poliovaccine was quite good although titres were low. Only 1 child without prior antibodies to type 1 failed to acquire them and all the children without antibodies to types 2 or 3 acquired them. Similarly, the response to diphtheria and tetanus was good. All the children responded to tetanus and all but 5 to diphtheria toxoid. A year later a booster dose was given to all the children; 41 were bled before the booster dose and 26 after. There had been a decline in the level of antibodies to poliovirus in the interval, 76%, 73% and 85% having antibody titres of more than 1:4 against types 1, 2 and 3 respectively. After the booster dose the median titre for all 3 types rose sharply from 8 to 512 for type 1, 16 to 512 for types 2 and 3, but 15% of the infants failed to respond to type 1, 4% to type 2 and 8% to type 3. All the infants responded satisfactorily to diphtheria and tetanus toxoids. Children with maternal antibody at the time of commencement of the immunization course showed a significantly lower percentage response to the complete immunization course than children without such antibody. This was most noticeable for the type 1 component and in the children aged 2–5 months.

The authors conclude that the quadruple antigen that they have prepared is satisfactory for use in large-scale immunization programmes but they note that the potency of the type 1 component should be improved. They also recommend that 3 doses each of 1 ml. should be used for the primary course to be followed a year later by a fourth booster dose. *A. J. Beale*

HOSPITAL AND OTHER CROSS INFECTIONS

WILLIAMS, R. E. O., JEVONS, M. Patricia, SHOOTER, R. A., HUNTER, C. J. W., GIRLING, J. A., GRIFFITHS, J. D. & TAYLOR, G. W. **Nasal Staphylococci and Sepsis in Hospital Patients.** *Brit. Med. J.* 1959, Oct. 10, 658–62. [10 refs.]

This work falls into two sections: section (1) determined the nasal carrier state of 602 hospital patients, the majority from a single 25-bed male surgical ward; section (2), relating nasal carriage to sepsis, analysed data from 1,358 patients in 4 wards during a period from September 1956 to April 1959.

(1) Of 602 patients swabbed within a few days of admission, 230 (38%) were nasal carriers of *Staphylococcus aureus* (coagulase-positive) and 80 (13%) possessed penicillin-resistant strains. Of 25 patients swabbed after 8 weeks' stay in the ward 17 (68%) were carriers and 13 (52%) had resistant strains. Of the patients who were non-carriers on initial swabbing, 30% acquired penicillin-resistant strains by the 3rd week, compared with only 18% of those who initially carried sensitive strains of *Staph. aureus*.

(2) Of 1,358 patients 722 had had surgical operations, 76 (5·6%) developed some staphylococcal sepsis during their hospital stay, 60 (4·4%) had some lesion other than wound sepsis and 34 (4·7%) post-operative cases had wound sepsis.

Of 342 patients who were never nasal carriers of *Staph. aureus* only 7 (2%) developed wound sepsis, whereas of 380 persons who were carriers, 27 (7·1%) developed staphylococcal wound sepsis. 18 of these 27 patients had the same type of staphylococcus in both nose and wound (in 3 cases the nasal staphylococcus was not isolated until after the onset of wound sepsis).

Assuming that all nasal carriers were, on average, equally at risk of acquiring autogenous wound sepsis, the authors analysed the "virulence" of hospital-acquired and penicillin-resistant strains. No more than a slight suggestion that these strains were more virulent was found. However, 7 (15·2%) of 46 patients who carried tetracycline-resistant strains developed wound sepsis due to their nasal strain, compared with only 11 (3·3%) of 334 patients who carried a sensitive strain.

The "local" virulent types of staphylococci were 47/53/75/77 +; 75/77 +; 75/77; 80; 6/42E/47/75vw; 187; 52/52A/80; 3C/71 +; 79 and 52/80. Of 26 patients who carried one of the above types in their nose, 9 (34·6%) developed post-operative sepsis due to the same type: conversely only 9 (2·5%) of 354 carriers of other types suffered sepsis.

Analysis of septic lesions other than wound infections showed closely similar rates of infection to those cited above, in carriers of the "local virulent" and other types of staphylococci and in non-carriers.

The authors stress the importance of acquisition in the nose of hospital strains of *Staph. aureus* in the genesis of wound and other sepsis, that self infection is an important factor in sepsis, and that sepsis might be reduced if nasal colonization could be prevented.

J. G. P. Hutchison

KRESKY, Beatrice & ELIAS, H. L. **Epidemiology of Staphylococcic Infection in Nursery of Small Community Hospital.** *J. Amer. Med. Ass.* 1959, Oct. 24, v. 171, No. 8, 1080–85, 3 figs. [18 refs.]

An epidemic of staphylococcal infection in a maternity hospital in Long Island, N.Y., apparently started with an infected episiotomy wound in a mother in January 1958. During the period up to May several infants were readmitted with sepsis and 1 mother had a breast abscess. Early in May 3 infants were readmitted and died, 2 certainly and the third probably from staphylococcal infection. At the same time there was a sudden increase in skin lesions among the babies in the nursery. Infected babies and their mothers were segregated; contaminated nurseries were cleaned and painted; nurses who were carriers were allowed to handle only the infected infants; and hexachlorophene soap was used for the babies. There was no decline in the incidence of infection. Segregation of infected and healthy babies was therefore strengthened and newly delivered mothers and babies were admitted to a separate unit; all infants were given 44 mgm. erythromycin per lb. body weight for 5–6 days; the babies were washed with hexachlorophene and later benzalkonium chloride; nurse carriers were treated with 1 gm. erythromycin per day for 4 days. There was a rapid decline in the number of infections seen in the nursery and only 3 new cases were found by later follow-up.

Subsequent questioning of physicians in the local community revealed 28 cases of infection in infants, with 3 deaths, and 8 infections in mothers, in a 7-month period. Cases of infection occurring at home seemed to be more severe than those developing in hospital.

In the discussion the authors emphasize the importance of proper ascertainment and recording of sepsis, and they recommend routine bacteriological investigation for carriers among nurses and infants, with exclusion of nurses who are carriers of the "nursery strain" of staphylococcus. [No type identification of the strains causing the epidemic is reported, so the conclusions on its aetiology must be speculative.]

R. E. O. Williams

FLECK, A. C., Jr. & KLEIN, J. O. **The Epidemiology and Investigation of Hospital-Acquired Staphylococcal Disease in Newborn Infants.** *Pediatrics.* Springfield, Ill. 1959, Dec., v. 24, No. 6, 1102–7. [26 refs.]

This is a general discussion of the epidemiology of staphylococcal infections in maternity nurseries. One of the authors' theses is that the onset of disease is determined almost entirely by the susceptibility of the tissues and little by the presence of the bacteria; the newborn is particularly susceptible. Potential sources of infection include infected personnel, especially those with lesions; infected infants in the nursery; and fomites including air. The evidence for the last is not impressive. The importance of epidemiological validation of sources implicated by bacteriological studies is emphasized.

R. E. O. Williams

HILL, A. M., BUTLER, H. M. & LAVER, J. C. **Reduction of Staphylococcal Infection in the Newly Born.** *Med. J. Australia.* 1959, Oct. 31, v. 2, No. 18, 633–4, 1 fig.

This is a valuable contribution to the prophylaxis of neonatal staphylococcal infection from the Infection Control Committee of the Royal Women's Hospital, Melbourne, where some 7,000 babies are born yearly. In 1956 the incidence of staphylococcal infection in the newly born was 1·9%, in 1957 it was 3·7%, and by October 1958 it was 17%. The use of hexachlorophene emulsion for all newly born babies was introduced in December 1958, and the effect was immediate and sustained. In the following 6 months, among 3,744 babies born in the hospital the staphylococcal infection rate was reduced to 1·3%; and the nasal carrier rate was also greatly reduced—from 90% to 30% in the 106 premature babies, and from 70% to 38% in the 111 full term babies examined. The technique was as follows:

Hexachlorophene emulsion 2 ml. was swabbed over the entire skin surface of the baby, especially on skin creases and natal clefts. The swabbing was then repeated with cotton wool moistened with warm water to obtain a lather. The lather was then wiped off with cotton wool till the skin was dry. An additional 1 ml. hexachlorophene emulsion was then wiped over the entire skin surface, and this second application was allowed to dry on the baby. *H. Stanley Banks*

COCCAL INFECTIONS

The order in this section is:—*Staphylococcus, Streptococcus, Neisseria, Others.*

KOCH, R., CARSON, M. J. & DONNELL, G. **Staphylococcal Pneumonia in Children. A Review of 83 Cases.** *J. Pediatrics.* St. Louis. 1959, Oct., v. 55, No. 4, 473–80, 7 figs. [24 refs.]

A striking increase in staphylococcal pneumonia was noted in 1956–58 in the Los Angeles Children's Hospital and 83 cases are reported. Empyema developed in 74 and pneumothorax in 42. Only 28 children responded to medical treatment alone: in the others surgical intervention was required—decortication, rib resection, lobectomy or tube drainage. Combinations of various antibiotics were used and bacitracin was regarded as the most useful. In 18 isolates tested the phage strain was 52-42B-81. 10 patients died, of whom 9 were under 4 months old. *A. B. Christie*

MORRIS, R. **Staphylococcal Pneumonia in Infants.** *Med. J. Australia.* 1959, Oct. 31, v. 2, No. 18, 625–9. [18 refs.]

Infantile staphylococcal pneumonia has in recent years become one of the commonest serious diseases seen in paediatric practice. 18 cases, all under 2 years of age, occurring in a children's ward in New South Wales over a period of 20 months are described. In only 5 cases (3 coagulase positive) was a staphylococcus isolated from throat swabs. The diagnosis largely depended on the clinical findings of respiratory embarrassment and on the X-ray findings of patchy consolidation and collapse, abscess cavities, or pleural effusion or tension cysts. The difficulty of obtaining the causal staphylococcus in cultures for diagnosis and antibiotic sensitivity tests is stressed; lung puncture is mentioned, but (as is too common in paediatric practice) routine blood culture does not seem to have been considered. The "appropriate" antibiotic for treatment is rarely penicillin in hospital practice, but all 5 of the strains isolated were sensitive to chloramphenicol. In this disease there should be continual seeking for pus in the pleural space, so that close drainage may be applied promptly. There were no deaths in this series. *H. Stanley Banks*

ISBISTER, Clair. **Staphylococcal Infection in Infancy.** *Med. J. Australia.* 1959, Oct. 31, v. 2, No. 18, 629–33, 4 figs. on pl.

This is a review from the Institute of Medical Research, Royal North Shore Hospital, Sydney, of this increasingly serious problem. Pertinent observations are made on the difficulties of diagnosis, even by X-ray, in the neo-natal period, and 22 cases of staphylococcal pneumonia in infants under 3 years of age are described, 5 of them in detail. In a further review of 69 cases, 30 were under 1 year of age and in only 9 of these was the diagnosis proved. In the series of 22 cases the organism was obtained from the sputum or laryngeal swabs in 7, from pleural fluid in 6, and from the lung *post mortem* in 5. [No mention is made of blood culture. When will paediatricians learn to do early routine blood cultures in febrile infections in which the diagnosis is in doubt?] *H. Stanley Banks*

BALDOVIN-AGAPI, Coralia, BADENSKI, Aurora, MIHALCO, Florica, IONESCO, Maria, CHIRESCO, Margareta & BORŞAI, Leia. Les staphylocoques pathogènes dans une collectivité d'écoliers, traités aux antibiotiques en vue de la prophylaxie de la maladie rhumatismale. [**Pathogenic Staphylococci isolated from a Collectivity of School-Children treated with Antibiotics**] *Arch. Roumaines Path. Expér. & Microbiol.* 1959, Sept., v. 18, No. 3, 435–45, graphs. [12 refs.]

An outbreak of streptococcal tonsillitis in a technical school of 500 pupils aged 12 to 18 years led to the use of penicillin and sulphonamides prophylactically for a month: carriers of haemolytic streptococci were given penicillin, the others sulphonamide. A study of the staphylococcal carrier situation showed that the percentage of penicillin-resistant strains rose during the month from 6·06% to 40%, and of sulphonamide-resistant strains from 18·66% to 87·36%. This was associated with an increase of staphylococci belonging to groups I and III. Of carriers of penicillin-sensitive staphylococci, 60% became negative during the month of prophylactic treatment. *A. B. Christie*

D'ANTONA, D. L'anatoxine staphylococcique en médecine humaine. (Bases doctrinales, préparation, contrôle et applications pratiques.) [**Staphylococcal Toxoid in Human Medicine**] *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd. Légale.* 1959, July & Oct., v. 17, Nos. 7 & 8, 543–65; 567–613, 6 figs. (4 coloured) on 4 pls. [697 refs.]

After a superficial discussion of the various toxins elaborated by staphylococci and in particular the action of the "α-toxin", which may be complex, on animal tissues it is concluded that the α-toxin is undoubtedly responsible for much of the pathogenic ability of the staphylococcus and this is supported by the assertions of numerous authors that the production of an immunity to the toxin has a beneficial therapeutic effect. There is a brief discussion of the relation of allergy to immunity. In the second part of the paper there is a general discussion of the methods of preparation and testing and administration of the α-toxoid. In discussing the applications of toxoid therapy the theme is "the staphylococcal toxoid constitutes a sovereign remedy for the conquest in a radical and definitive way, of staphylococcal infections, achieving a percentage of cures which exceeds 90% of cases". The recommended dosage comprises a course of 8 injections increasing from 0·1 to 1·5 ml. over 20–25 days; in the case of reactions the dosage should be reduced but the injections continued to effect a desensitization. Later booster doses may also be required.

[This is an entirely dogmatic review by a vigorous advocate of toxoid therapy for staphylococcal infections, supported by 697 references, but giving hardly any indication of the scientific evidence available to support this advocacy.] *R. E. O. Williams*

KIRBY, W. M. M., PERRY, D. M. & BAUER, A. W. **Treatment of Staphylococcal Septicemia with Vancomycin. Report of Thirty-Three Cases.** *New England J. of Med.* 1960, Jan. 14, v. 262, No. 2, 49–55, 4 figs. [10 refs.]

The activity of vancomycin against staphylococci depends on the facts that staphylococci are uniformly susceptible and resistance develops slowly if at all, that the drug is bactericidal and that high serum and tissue concentrations can be obtained. Its main disadvantage is that it must be given by intravenous infusion—0·5 gm. is diluted in 10 ml. saline and added to 100–200 ml. of 5% glucose, the recommended dose being 1·0 gm. twice daily. Chills, fever and rashes may occur but can be allayed by the addition of 20 mgm. hydrocortisone to the infusion. In the present series of 33 cases the septicaemia was eradicated and the patient cured in 20 instances: in 6 the infection was overcome but the patient died from underlying disease: in 7 the treatment was not successful. Most of the patients had severe underlying disease and 13 were over 70 years old. Of 14 patients infected outside hospital, 9 had a staphylococcus resistant to penicillin and of 19 infected in hospital, 18 had a staphylococcus resistant to more than 1 antibiotic. 4 cases histories are presented in detail.

[This is an article worth studying in the original.] *A. B. Christie*

ABBOUD, F. M. & WAISBREN, B. A. **Correlation between *in vitro* Studies and Response to Antibiotic Therapy in Staphylococcic Bacteremia.** *Arch. Intern. Med.* 1959, Aug., v. 104, No. 2, 226–33, 7 figs. [24 refs.]

This paper is based on 100 cases of staphylococcal bacteriaemia treated at Milwaukee County Hospital in 1952–57. The results of treatment, which are classified as "response", "indetermined" or "no response", are compared with the sensitivity of the staphylococcus to the antibiotic used as determined by a tube dilution test. It is concluded that if the organism grows in 6 μgm./ml. or more of any antibiotic, a therapeutic response is not to be expected.

Of 81 patients treated with penicillin, only 18 responded; the staphylococci from all these were inhibited by 3 μgm./ml. or less: there were 11 other strains in this category from patients with an indeterminate or no response. All others were more resistant and most of these patients died. Chloramphenicol was given to 53 patients: only 4 responded, their organisms being inhibited by 6, 6, 12 and 38 μgm./ml., many of the remainder being more resistant. Erythromycin produced a response in 14 out of 43 patients, all of whose organisms were inhibited by 3 μgm./ml. or less. Tetracyclines produced a response in 15 out of 41 patients: in one of these the minimum inhibitory concentration was 6 μgm./ml. and in the remainder less. The results with novobiocin, neomycin and vancomycin were less numerous and vitiated by resort to these antibiotics for "nearly terminal patients". Positive blood cultures after treatment had started were obtained in 66 patients with infections resistant by this definition, and in only 3 with sensitive infections. It is suggested that to avoid the labour of a complete tube dilution test a simple determination of whether the organism is inhibited by 6 μgm./ml. could be used as a guide.

[This is valuable evidence of the significance of sensitivity tests. On the other hand, the dividing line cannot be the same for all antibiotics: the concentrations of penicillin or novobiocin obtainable in the blood are much higher than those of tetracycline or erythromycin. In tests of sensitivity to penicillin the technique of the test proposed will need to be carefully standardized, since the result depends so largely on the size of the inoculum and hence on the amount of preformed penicillinase added.] *L. P. Garrod*

KIRSCHNER, L., MARKHAM, N. P. & WATTERS, P. A. **Streptococcal Infections in Tropical Regions.** *New Zealand Med. J.* 1959, Aug., v. 58, No. 326, 491–4.

Previous work by the authors in Java and Raratonga (Cook Islands) showed a high carrier rate of Group A streptococci (36·9% in Java) and a low rate of severe streptococcal disease. It was thought that this was due to an early acquired immunity to this organism. As an indication of recent streptococcal infection therefore, antistreptolysin titres were estimated on sera of 203 Maoris living in Raratonga and compared with titres

in sera of 127 healthy New Zealand Maoris and 150 Europeans.

Antistreptolysin titres were found to be raised in 88·6% of Raratongan sera: over 60% of them had titres of 500 units/ml. or more. The highest percentage was in the 5 to 10 year age-group. 45·5% of New Zealand Maoris had raised titres compared with 4% of Europeans. This difference was thought to be due to the prevalence of streptococcal skin lesions in Raratongans and the authors suggest that early infections are accompanied by the development of type specific immunity (as well as antibody to streptolysin O) which accounts for the low rate of severe streptococcal disease in adults. *M. Patricia Jevons*

CLARKE, C. A., MCCONNELL, R. B. & SHEPPARD, P. M. **ABO Blood Groups and Secretor Character in Rheumatic Carditis.** *Brit. Med. J.* 1960, Jan. 2, 21–3.

Data are presented regarding ABO blood grouping and secretor status of 263 Liverpool patients suffering from rheumatic carditis. There was a significant reduction in the incidence of blood group O and a non-significant increase in non-secretors compared with controls. Combining their figures with some supplied by other workers, the authors find a significant difference in both factors. They feel that the figures suggest a relationship between ABO blood group antigens and rheumatic fever but that further data are required both from rheumatic fever patients and those suffering from streptococcal throat infections and acute nephritis.

[See also this *Bulletin*, 1959, v. 34, 1252.]

A. B. Christie

HORSTMAN, H. A., Jr. **Oral Penicillin V Therapy in Treatment of Patient with Bacterial Endocarditis.** *Antibiotic Med.* New York. 1960, Jan., v. 7, No. 1, 41–3.

Successful treatment of a penicillin-resistant *Streptococcus viridans* endocarditis with oral penicillin in a patient with a history of penicillin reaction is described.

BACTERIAL INFECTIONS

The order in this section is:—*General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.*

DE WEVER, A. & HEYNE, D. Rapport général sur l'endémie diphtérique en Belgique. [**Report on Diphtheria Endemicity in Belgium**] *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd. Légale.* 1959, Nov.–Dec., v. 17, Nos. 9/10, 671–86, 2 graphs (1 folding).

Belgium, in common with other European countries, experienced a rise in the incidence of diphtheria during the war. The number of cases rose from 2,311 in 194 to a maximum of 16,157 in 1943 and the number o deaths increased from 403 to 982. The notification fell to a minimum of 512 in 1951 with 53 deaths. Th incidence then rose slightly and over 600 cases wer recorded annually during 1953–6 but the mortality fell only 20 deaths were recorded among 647 cases in 195 In 1957 the number of cases rose to 879 and in 195 to 1,312. This rising trend is in contrast to the experi ence of other countries where the fall has been con tinuous in recent years. Children aged 15 years an under formed 82·5% of all cases in 1958.

The numbers immunized against diphtheria varie considerably from year to year and between differen areas. For the whole country the number vaccinate rose from 31,688 in 1956 to 77,584 in 1957 but thi rise was almost wholly due to the area of West Flander where the vaccinations rose from 3,862 to 53,749. Th total immunized in 1958 fell to 53,809. The areas o Antwerp, Mons, Charleroi, showed an increase o 29,384 immunizations in 1958 while Brabant, Liège East and West Flanders showed a fall of 53,499. I Limbourg there were 12,990 vaccinations in 1955 bu only 280 and 470 in 1957 and 1958.

Concern for the present trend of diphtheria i Belgium and the necessity for immunization has bee expressed by the Minister of Health in a circular lette to members of the medical profession. *W. J. Martin*

OLITZKI, Z. **Epidemiological Observations on Diphtherial Infection in Jerusalem. II. Results obtained from Laboratory Reports of the Central Government Laboratories.** *Acta Med. Orientalia* 1958, v. 17, Nos. 5/6, 101–10.

A summary of Part 1 of this paper appeared in thi *Bulletin*, 1959, v. 34, 855. The present section cover 1948–57 and during this period the throat sample positive for diphtheria numbered 829 for the Centra Government Laboratory and 189 for the Hadassa Medical Organization and the samples from the nos and non-pharyngeal sites positive for diphtheria wer 516 and 111, respectively. Before 1948 almost all o the positive results were obtained from the pharynx The change is due partly to the increased interest i non-pharyngeal infections resulting in more sample being tested, and partly to a different outlook on diph theria, more attention being paid to prevention. All types of infection have a similar seasonal distribution a summer minimum and a maximum in October. Th non-pharyngeal cases occurred at younger ages tha the pharyngeal, 67·5% of the former and 24·5% of th latter were in the age-group 0–2 years.

[Unfortunately there are some discrepancies in th values given in the text and tables. The non pharyngeal cases in the baby homes are given as 4·5% in the text and 6·0 in Table IV but the actual valu found from Table III is 44·9. The pharyngeal infec tions sent in from medical officers of sick funds i given as 45·0% in Table IV but from Table II th value should be 6·9, and the value for baby home should be 6·0 instead of 6·6.] *W. J. Martin*

SCHWIMMER, R. **Primary *H. influenzae* Pneumonia in an Adult with Extreme Hyperpyrexia.** *Amer. J. Med. Sci.* 1959, Dec., v. 238, No. 6, 713–19, 2 figs. [15 refs.]

This is a record of an illness in a 49-year-old negress in whom blood culture grew *Haemophilus influenzae* on 2 occasions and X-rays showed consolidation in the right lung. On the day of admission, temperature rose to 108·2°F. but subsided after the administration of cortisone. A later symptom was severe pain in the muscles of one leg. The patient was treated with streptomycin for 10 days and sulphonamide was added during the last 7 days: tetracycline was added at the end of treatment "to obviate the possibility of residual infection or recurrence". *A. B. Christie*

HUMBERT, R., MANNWEILER, E. & SIEMENS, W. Typhöse und gastroenteritische Salmonellosen. [**Salmonella Infections—Typhoid and Paratyphoid Fevers and Gastro-Enteritis**] *Deut. med. Woch.* 1960, Jan. 29, v. 85, No. 5, 185–92, 211–2, 4 figs. [63 refs.]

This paper contains an account of the diagnostic and therapeutic experience in 308 cases of salmonella infection which were observed in the period 1954–6 at the General Hospital, Altona. The types of *Salmonella* isolated are recorded in a table and those most frequently found were *Salm. paratyphi B* (92 cases), *Salm. Thompson* (56 cases which were mainly due to a group infection by contaminated imported dried egg), *Salm. typhi* (52 cases) and *Salm. typhi-murium* (50 cases).

The analysis of the cases is described and the findings are set out in tables which cover (1) the day of disease on which salmonellae were first recovered from blood or faeces, (2) the picture of the disease whether it was that of typhoid, gastro-enteritis, or of a mixed form or was asymptomatic, (3) the complications which occurred in the infections by different salmonellae and (4) the causes of death in the 10 fatal cases.

In the treatment chloramphenicol was found to be most effective in typhoid and paratyphoid infections: it was also the drug of choice in the more severe cases of gastro-enteritis. Mild cases of gastro-enteritis responded well to sulphonamide treatment. The problem of "bacteriological cure" was also considered and it was found that this could not be ensured either by chloramphenicol, tetracyclines or sulphonamides but that penicillin in a daily dose of 17 million units for 5 days proved to be the best for the purpose of this cure. *M. E. Delafield*

TEIXEIRA, R. dos S. Estudo clínico de casos de febre tifóide prolongada. [**Clinical Study of Cases of Prolonged Typhoid Fever**] *Bol. Depart. Saúde.* Bahia. 1959, Jan.–June, v. 3, No. 1, 5–145, numerous figs. [126 refs.] English summary.

This is a monograph of 145 pages in Portuguese, with an English summary and conclusions running to 32 short paragraphs. The 12 patients investigated all contracted typhoid fever during an epidemic in Teotonio, Bahia, in 1957. They were selected for study because of the long-standing fever and accompanying illness varying in duration from 6 to 11 months, characterized by diarrhoea, non-productive cough, severe loss of weight, amenorrhoea, paleness, enlargement of liver and spleen, and ecchymoses. None of the classical complications of typhoid fever, such as intestinal haemorrhage or perforation, cholecystitis, bronchopneumonia, etc., occurred in these cases. There were 8 females and 4 males of age-range 5 to 35 years (average 15), and 10 were white and 2 mulatto. There were no deaths, and some 8 months after completion of treatment the patients were in good general and nutritional condition, with regression in the size of the liver and spleen.

The usual clinico-pathological examinations were done, but conclusive findings were few, probably because the examinations were mostly made at a late stage of the disease. Stool cultures were positive for *Salmonella typhi* in 3 out of 11 patients examined, blood cultures positive only in 2 cases, and Widal reactions showed high titres of H agglutination in all cases, and recognizable O titres only in 3 cases. Liver biopsy showed invasion by all types of leucocytes, congestion, and fatty infiltration; no parasites were seen. Ova of *Schistosoma mansoni* were found in the stools of 88·8% and of *Ascaris lumbricoides* and *Trichuris trichiura* in all the patients; 44·4% had ova of hookworm. The skin test for schistosomiasis was negative in 8, doubtful in 1, and weakly positive in 3.

Clinically the disease could be said to resemble kala azar, but no leishmaniae were found. Chloramphenicol treatment, combined with 2 doses of antityphoid vaccine at an interval of 7 days, was given and the response was said to be good in almost all cases; there was only 1 relapse and the patient responded rapidly to additional chloramphenicol.

The clinico-pathological picture described here is very different from that of severe cases of pure typhoid fever, and the modifications observed may well have been due to associated chronic diseases, particularly schistosomiasis. *H. Stanley Banks*

MILLER, A. A., NICOL, C. G. M. & RAMSDEN, F. **A Prolonged Infection with *Salmonella bovis-morbificans*.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Jan., v. 19, 2–7, 7 diagrams.

DORDEVIC, R., JOKANOVIC, D., KRAJINOVIC, S., SRETENOVIC, M., VASILIC, M., UDICKI, S. & ZDRAVKOVIC, A. Prilog ispitivanju hronične dizenterije. Bakteriološka, parazitološka, epidemiološka, anatomopatološka i histopatološka istraživanja. [**Contribution to the Study of Chronic Dysentery. Bacteriological, Parasitological, Epidemiological, Anatomopathological and Histopathological Investigations**] *Acta Med. Iugoslavica.* 1959, v. 13, No. 1, 84–113, 10 figs. [42 refs.] English summary.

Material from 907 autopsies carried out in Belgrade in 1956 and 1957 on persons who had died from various causes was examined with the object of detecting cases of

chronic dysentery and investigating the histopathology and bacteriology of this condition. Dysentery bacilli were isolated in 25 (2·8%) and *Entamoeba histolytica* in 13 (1·4%) instances, and lesions indicative of dysentery in spite of negative bacteriological findings were observed in 54 (5·9%) instances. The total number of cases of chronic dysentery was thus 92 (10·1%). *Shigella flexneri* was isolated most frequently (21 strains, including 11 of type 2), and *Sh. dysenteriae, Sh. boydii* and *Sh. sonnei* were also found. *D. J. Bauer*

Lányi, B., Szita, J., Ringelhann, B. & Kovách, K. **A Water-Borne Outbreak of Enteritis associated with *Escherichia coli* Serotype 124: 72: 32.** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 1, 77–84, 1 fig. [10 refs.]

This paper describes the investigation of 24 cultures of *Escherichia coli* isolated from 107 faeces specimens during an epidemic of mild diarrhoea affecting 255 persons in and near a children's holiday camp in Hungary in July 1958. The 24 strains were found to be identical with Ewing's strain 227 and to have the formula O124 : K72(B17) : H32. The epidemic was caused by a local mineral spring becoming contaminated by a defective sewer pipe from the camp—the original carrier was not detected. No significant agglutinins were found in sera from 25 patients—the authors presume that this was probably because the infection was of very short duration (a few days).

John S. Stevenson

Aznar Reig, A. & López, A. **Exanthem in Brucellosis treated with Novobiocin.** [Correspondence.] *Lancet.* 1959, Nov. 28, 972–3, 1 fig.

The authors write from Cadiz, Spain. They treated 45 patients with brucellosis, giving 1·5 gm. novobiocin daily for 10 days and 1 gm. for 5 days; half the patients developed an acute, widespread and irritating rash, with high fever, at about the 8th day. Anti-allergic drugs and prednisone were not helpful. Some patients developed intense local oedema; one developed a haemorrhagic condition with haematuria.

This complication of treatment alarmed the patients, and made the position more difficult; moreover, the disease relapsed in 40% and the drug was no more beneficial than other antibiotics; there is therefore no indication for its use in brucellosis.

Charles Wilcocks

Tompkins, A. B. **Tetanus in African Children.** *Arch. Dis. in Childhood.* 1959, Oct., v. 34, No. 177, 398–405, 2 figs. [40 refs.]

This is a critical analysis of 79 cases of tetanus occurring in African children, other than neonates, in Ibadan, Nigeria. The usual points of interest are discussed, *e.g.* incubation period, age, sex, site, period of onset. Otogenic tetanus, in which trismus and risus sardonicus were severe in proportion to spasms, occurred in 21 patients. The effect of differing doses of antitoxin is discussed; there was no significan difference between the effects of small and large dose and reference is made to a trial now going on in whic no antitoxin is given to some patients.

[This is a good critical article with many references.

A. B. Christie

Nuti, M. Considerazioni statistico-cliniche su 89 ca di tetano occorsi nella zona di Fano nel ventenni 1938–1958. [**Clinico-statistical Observations o 89 Cases of Tetanus Encountered in the Zone o Fano in the 20-year Period 1938–1958**] *Arch Ital. Sci. Med. Trop. e Parassit.* 1959, Oct., v. 4 No. 10, 533–44. [19 refs.] English summary.

The author analyses 89 cases of tetanus, encountere in hospital between 1938 and 1958, with respect to ag sex, season, occupation and site of wound. Mortalit has remained almost stationary in the 20-year perio though there was an increase from 30·2% to 36·9 after the introduction of antibiotics: the authors ca find no reason for this difference. *A. B. Christie*

Sujoy, E., Shepherd, Gwendolyn, Simsolo, Victoria Peries, J. & Ezkenazi, J. El tétanos en el niñ Diez anos de experiencia. [**Tetanus in the Chil Ten Years' Experience**] *Semana Méd.* 1959, Oc 29, v. 115, No. 18, 703–8, 4 figs.

This is a review of 132 cases of tetanus in childre in Buenos Aires analysed according to age, sex inc bation period, site of entry and symptomatolog The mortality in neonates (37 cases) was 81·6%. Th total mortality was 43·2%. There has been no obviou improvement in results of treatment over the 10 yea and the authors feel that the main hope of diminishi the disease lies in compulsory immunization.

A. B. Christie

Rafyi, A. & Maghami, G. Sur la fréquence de lept spirose en Iran. Isolement de *Leptospira grippo typhosa* chez l'homme et chez les bovins. [**Inc dence of Leptospirosis in Iran. Isolation of *grippotyphosa* from Man and Cattle**] (2e note *Bull. Soc. Path. Exot.* 1959, Sept.–Oct., v. 52, No. 592–6.

Welshimer, H. J. & Winglewish, Nancy G. **Listeri sis—Summary of Seven Cases of Listeria Men ingitis.** *J. Amer. Med. Ass.* 1959, Nov. 7, v. 17 No. 10, 1319–23. [16 refs.]

Listeria monocytogenes was first isolated in 192 1924, from rabbits and guineapigs, and in 1932 fro patients with an infectious mononucleosis syndrom The organism is being increasingly found, especially Germany and the United States, predominantly patients suffering from meningitis, but also in oth conditions including granulomatosis of the foetus an

newborn infant, conjunctivitis, endocarditis, urethritis, and a type of infectious mononucleosis. The disease is probably more common than is supposed, the diagnosis often being missed because of the morphological resemblance of *L. monocytogenes* to a non-pathogenic diphtheroid. The mode of transmission is unknown, but there is some evidence that the infection may be spread by ticks.

7 cases of meningitis are described from Richmond, Virginia, the last 6 having been discovered during a period of 13 months. 2 were infants of 9 and 14 days old respectively, 1 was a child of 10 months, and the remainder were adults in the age range 47–64. Both the infants died, and one of the adults was discharged with residual brain damage. The others recovered rapidly under treatment with penicillin plus chloramphenicol or a sulphonamide. All 7 strains isolated from the spinal fluids were sensitive to the 5 antibiotics with which they were tested *in vitro*.

In this form of meningitis the spinal fluid is usually opalescent but not purulent. The total white cells in the fluid in these 7 cases ranged from 143 to 2,409 per cmm., and the polymorphonuclears from 13 to 80%.

H. Stanley Banks

McCarty, D. & Bornstein, S. **Erysipelothrix Endocarditis. Report on a Septicemic Form of the Erysipeloid of Rosenbach.** *Amer. J. Clin. Path.* 1960, Jan., v. 33, No. 1, 39–42, 2 figs.

"A 50-year-old butcher with a history of alcoholism was admitted to the hospital as a result of decompensated hepatic cirrhosis. He manifested mild evidence of valvular disease of the heart and a noncharacteristic skin eruption. Thirteen days later, after an initial regression of symptoms, he had a febrile episode of sudden onset, characterized by increased heart murmurs and pretibial petechiae; *Erysipelothrix insidiosa* was cultured from his blood on 3 occasions. The patient became afebrile and improved generally after therapy with penicillin. Infection with Erysipelothrix, if thought of, can be easily diagnosed. Much has to be learned regarding the epidemiology of this infection in man, especially through progress in finding cases."

VIRUS INFECTIONS

The order in this section is:—*General, Psittacosis-Lymphogranuloma group, Pox group, Respiratory group, Enteric group, Arthropod-borne group, Others.*

Bolande, R. P. **Inclusion-Bearing Cells in the Urine in Certain Viral Infections.** *Pediatrics.* Springfield, Ill. 1959, July, v. 24, No. 1, 7–12, 3 figs. (1 coloured). [11 refs.]

Examination of the fixed and stained urinary sediments from children during an epidemic of viral infections in the Cleveland area revealed the presence of cells containing discrete cytoplasmic inclusions suggestive of viral inclusion bodies. These were found in 16 out of 20 patients with measles, mainly in the prodromal and early eruptive phase, in 3 of 4 with rubella, in 4 of 5 with chickenpox, in 2 of 2 adults with mumps, in 4 of 5 patients with herpangina and 1 of 4 with aseptic meningitis. In 82 controls, either well or suffering from nonviral infections, they were present in 15 but were usually very sparse. The presence of large numbers of these cells is characteristic though not diagnostic of measles. The inclusions may represent the cytopathic effects of viral infections on cells derived from the blood or urinary tract stroma and their presence may help towards a further understanding of the pathogenesis of viral exanthemata in human beings.

A. B. Christie

Freud, P., Maffia, A. J., Hosbach, R. E. & Valicenti, P. W. **Smallpox Vaccination followed by Acute Renal Failure.** *J. Dis. Children.* Chicago. 1960, Jan., v. 99, No. 1, 98–100. [26 refs.]

On the 12th day of a successful primary vaccination a female infant aged 8 months developed symptoms of anaphylactoid purpura (Henoch's). Some 12 hours later the child became anuric and remained so for 5 days. After recovery the patient remained free from symptoms over a period of 2 years, but albumin, low specific gravity and occasional granular casts have persisted in the urine. Allergy to food, drugs and vaccinia were considered as possible causative factors in this case. Diet had lately been unvaried; aspirin and penicillin, the only drugs involved, had both been given previously without any evidence of hypersensitivity.

The authors found in the literature a number of instances of renal complications, but only one case of acute failure, following vaccination.

J. Pickford Marsden

Partington, M. W. **An Illness of Infection in Chickenpox.** [Correspondence.] *Lancet.* 1960, Jan. 16, 172, 1 fig.

"Illness of infection" may occur during the primary viraemia which is thought to occur soon after the local invasion of the body by a virus [Fenner, this *Bulletin*, 1949, v. 24, 372]. Such illness has been described in the case of measles by Goodall (*Clin. J.*, 1925, v. 54, 69).

Temperature records for 15 days were kept of 5 close family contacts of a boy who had developed chickenpox. The father, who had had the disease, remained afebrile throughout. Each of the others developed chickenpox in due course. The mother ran a temperature of 99·6°F. on the evenings of the 3rd and 4th days of the boy's illness. During the same period the other 3 children had at least one temperature recording of 99°F. but without any symptoms. In 2 of these children, and in the mother, the temperature thereafter remained down until the fever associated with the appearance of the rash. In the 3rd child, however, the temperature rose to 99°F. or over on the 3rd, 4th, 7th and 10th days of the incubation period.

J. Pickford Marsden

PORTER, I. H. & PALLIS, C. **Polyneuritis and Central Hypertension due to Non-Parotitic Mumps.** *Lancet.* 1960, Feb. 13, 362–3. [14 refs.]

This is a report on the occurrence in a woman aged 17 of severe polyneuritis followed by meningoencephalitis with central hypertension. The diagnosis of mumps rested on serology: V and S antibodies were raised to 1/64 and 1/32 respectively and both fell to 1/8. [The woman had apparently been in hospital for 10 weeks before the onset of the polyneuritis but there is no history of exposure to mumps or of its occurrence in other patients or staff.] *A. B. Christie*

CANDLER, Marguerite L., COOPER, G. R., KOKKO, U. P., ROBINSON, R. Q. & WILLIS, M. J. **Intradermal Vaccination in Healthy Adults with Type A Asian Strain Influenza Vaccine.** *Proc. Soc. Exper. Biol. & Med.* 1960, Jan., v. 103, No. 1, 151–4.

"The immune response elicited by 2 intradermal injections of 0.1 ml monovalent Asian A influenza vaccine administered 2 weeks apart was related to the antigenic potency of the vaccine. Individuals developing detectable antibodies 2 weeks after the second injection varied with dose from 44 to 70% with titers 1:40 or greater. Using the same lot and dosage schedule of vaccine an intradermal booster immunization administered 53 weeks after first vaccinations, induced marked rise in titers which were also related to dose. The geometric mean titers which ranged from 1:21 to 1:51 two weeks after second injection of vaccine rose to 1:51 to 1:211, 2 weeks after booster injection. In the present study, 2 separate injections of 50 CCA units resulted in better antibody responses than single injections of 100 CCA units. Even the response to 2 injections of 12.5 CCA units is as good as the response to single doses 4 times as large. Systemic and local reactions increased with unit dose of vaccine but no serious reactions occurred with the lot of vaccine used throughout this study."

ZHDANOV, V. M. & RITOVA, V. V. **Evaluation of the Effectiveness of Live Influenza Vaccines.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 4, 472–9.

Attenuated strains of influenza A, A-prime and B were administered intranasally to 1,050 children 1–3 years old and to 132 adults. A small proportion of adults reacted with mild clinical symptoms including slight pyrexia in 1–2% of subjects. Clinical reactions observed among children were more frequent, with temperatures of 99·6° or higher in 5% and local symptoms in 15%. Virus isolations from naso-pharyngeal secretions collected 1 to 5 days after inoculation gave positive results in 50 to 90% of adults and in 90 to 100% of children. This was accompanied by frequent antibody rises estimated by haemagglutination-inhibition. A second virus dose administered 1 to 4 months after the first failed to establish infection but frequent "takes" were observed following a third or fourth dose given at 6 months' intervals. Evidence is pre sented to show that simultaneous vaccination with different types of attenuated strains resulted in cor current infection by each of the viruses used wit corresponding antibody rises. Transmission of infectio from vaccinated children to normal contacts wa observed but no evidence could be detected c secondary spread from infected contacts.

Criteria adopted for evaluating the efficacy of liv influenza vaccines are discussed. *H. G. Pereira*

GINSBERG, H. S. **Newer Aspects of Adenovirus In fections.** *Amer. J. Pub. Health.* 1959, Nov., v 49, No. 11, 1480–85. [41 refs.]

This is a review of the progress made in the las 4 or 5 years in identifying the types of adenoviru associated with particular diseases, and especially the role in the aetiology of acute respiratory infection 23 immunologically distinct types have now been re cognized, 18 of which are of human and 5 of monke origin. The most common disease syndromes an associated types are: non-bacterial pharyngitis, types and 7; pharyngoconjunctival fever, type 3; conjunc tivitis, types 3 and 7; acute respiratory disease (ARD types 4 and 7; epidemic keratoconjunctivitis, type Serum antibody studies in the civil population indica that over 50% of children under 3 years have alread been infected with types 1 and 2, apparently witho clearly defined illness, and that types 3 and 7 antibodi are found in some 20–50% of adults.

As regards association with definite clinical illnes the first 7 types may be classified into 2 sub-groups (a) types 3, 4, and 7 as major causal agents of disease and (b) types 1, 2, 5, and 6, as not associated wit epidemics, although they may cause sporadic illnes A sharp distinction can be made between civil an military populations in this respect. In the former onl about 1·5 to 4% of acute viral respiratory disease attributable to adenoviruses, type 3 being the principa offender; among recruits of a few months' standing however, adenovirus infections can be a highly impo tant source of acute respiratory illness, especially typ 4 and 7. On the other hand, the incidence of adeno virus illnesses among seasoned troops falls approx mately to civilian level. *H. Stanley Banks*

KAUFMANN, G., WEGMANN, T., RENTSCH, M. & WIES MANN, E. Adenovirusinfektionen Typ 4 und 7a i der Ostschweiz 1958. Klinische, virologische un serologische Untersuchungen. [**Types 4 and 7 Adenovirus Infections in Eastern Switzerland i 1958. Clinical, Virological and Serological In vestigations**] *Schweiz. med. Woch.* 1959, Aug. 2 v. 89, No. 34, 877–82. [68 refs.]

The authors have observed 32 cases of adenoviru infection which occurred in eastern Switzerland in 195 In 12 civilians and 11 army recruits the onset was acut with fever lasting 5–6 days, in some cases with head ache, vomiting, meningism, pharyngitis, conjunctivit and cervical lymphadenitis. The disease generall resembled pharyngoconjunctival fever. Adenovirus

type 7a was isolated from 1 patient and serological investigations indicated that the outbreak was due to types 4 and 7a. In 9 other patients infiltrations were observed in the lungs. *D. J. Bauer*

Wegmann, T., Kaufmann, G. & Wiesmann, E. Lungeninfiltrate bei Adenovirusinfektionen. [**Infiltration of the Lungs in Adenovirus Infections**] *Schweiz. med. Woch.* 1959, Aug. 22, v. 89, No. 34, 882–7, 5 figs. [50 refs.]

The 9 cases of lung involvement associated with adenovirus infection mentioned in the preceding paper are described in further detail. 6 patients were recruits; 4 had suffered from a respiratory infection 7–8 weeks previously, and all were apparently fit for duty at the time of routine X-ray examination at the end of their military service. Investigation of the chest at this examination showed enlargement of the hila and diffuse opacities in the lower lobes. The remaining 3 patients were civilians, and the involvement of the lungs was detected shortly after the onset of an adenovirus infection which pursued a typical febrile course. The diagnosis was established in all cases by complement-fixation tests. Transient unspecific positive results in Wassermann tests and orinthosis complement-fixation tests were observed. *D. J. Bauer*

Tateno, I.; Sugiura, A.; Suzuki, S.; Morita, T.; Kitamoto, O.; Togashi, M.; Suzuki, K.; Kaneko, Y.; Kawashima, A.; Sato, T.; Obara, S.; Kasai, N. **Current Experiences in the Serological Diagnosis of Primary Atypical Pneumonia and Related Illnesses with a Battery of Antigens. I. Current Status of the Diagnostic Value of Cold Hemagglutinin** [Tateno, Sugiura, Suzuki, Morita, Kitamoto, Togashi, Suzuki, Kaneko, Kawashima, Sato & Obara]. *Japanese J. Exper. Med.* 1959, Oct., v. 29, No. 5, 457–70, 4 figs. [Numerous refs.] **II. Diagnostically Complicated Cases** [Tateno, Suzuki, Kitamoto, Togashi, Suzuki, Kaneko, Obara, Sato & Kasai]. *Ibid.*, 471–80, 19 figs. on 3 pls.

I. Infection with cold-haemagglutinin-inducing agents (CHA-IA) may lead to the development of pulmonary infiltrations but also to mild respiratory disorders or to subclinical states. A high titre of cold haemagglutin antibody (CHA) in association with primary atypical pneumonia (PAP) is not therefore diagnostic: only a 4-fold rise during the illness can be so regarded. A high but level titre of CHA associated with PAP may represent a state in which infection with CHA-IA has been going on for a month or so in the patient till some other factor induces the pneumonic process.

II. Case histories of 13 patients with pulmonary infiltrations are studied in relation to serum reactions to a battery of antigens. The authors feel that the importance of CHA titres has been exaggerated by some physicians and that only when a rise in titre occurs between acute and convalescent samples of sera can much weight be given to the findings. Even then simultaneous infections with other agents, *e.g.* influenza A virus and the tubercle bacillus may be present. Infiltrations lasting more than 6 weeks should not be ascribed to infection with CHA-IA. *A. B. Christie*

Nicolau, S. S., Biberi-Moroianu, S. & Cajal, N. Cîteva date statistico-epidemiologice asupra evoluţiei hepatitelor epidemice inframicrobiene în Romînia. [**The Epidemiology of Epidemic Hepatitis in Rumania**] *Studii si Cercetări Inframicrobiol.* 1959, v. 10, No. 4, 401–16, 3 figs. [28 refs.] French summary.

The authors discuss records of the disease as far back as 1784, but in detail for the period 1952–58; it was made notifiable in 1952. In this period the incidence has increased slowly in spite of improvements in sanitation. At first it was an urban disease, but recently it has spread into the rural areas, though the greatest incidence remains in the densely populated districts. There is a peak of incidence in November and December but the difference between this and the general level is slight, which indicates a high degree of endemicity. Unlike most other infections it affects mainly adults, but in recent years there has been an increase in patients aged 7–14 years, especially in the last quarter of the year after re-assembly at school.

The authors discuss the possible influence of mode of living and diet on the disease, and the possible role of parenteral infection, which, however, could not account for the increase in incidence.

Charles Wilcocks

Schön, H., Englisch, B. & Wüst, H. Serumfermentuntersuchungen bei einer Hepatitisepidemie. [**A Study of Serum Enzymes during an Epidemic of Hepatitis**] *Deut. med. Woch.* 1960, Feb. 12, v. 85, No. 7, 265–7, 4 figs. [13 refs.]

There are as yet few reports in the literature on the use of methods for the study of serum enzymes in the diagnosis of cases of non-icteric epidemic hepatitis. Such cases are of particular importance since they occur particularly in children in whom the disease may not be diagnosed. Recognition of all cases is not only of epidemiological importance but also because of the risk of the acute form of the disease becoming a chronic form with danger of hepatic cirrhosis.

The work described in this paper consisted in the attempt to determine the frequency of non-icteric hepatitis during an endemic of infective hepatitis among the population of a village about 1,800 in number. Up to the present 166 cases of infective hepatitis have been diagnosed (152 children and 14 adults) and of these 94 were established on the results of serum tests. The tests employed were: (1) Enzyme activity tests—(i) glutaminic-acid—oxalacetic-acid transaminase, (ii) glutaminic-acid—pyruvic-acid transaminase, (iii) sorbite dehydrase, and (iv) lactic acid dehydrase; (2) Lability tests—(i) Takata reaction and (ii) thymol turbidity test; (3) Bilirubin concentration; (4) Paper electrophoresis of protein fractions.

In a description of the results of these tests in the 94 cases it is stated that definite jaundice as judged on the bilirubin test and clinical observation was present in only 23%. The opinion is expressed that the enzyme tests and particularly the glutaminic-acid—pyruvic-acid transaminase test are of great value in the diagnosis of non-icteric infective hepatitis and also in the assessment of the degree of recovery after the acute attack. In 166 cases of the disease the findings of serum enzyme tests had not returned to normal in 20 of these even after 2 months or more, which makes it probable that the disease had taken on a chronic form.

M. E. Delafield

BANG, N. U., RUEGSEGGER, P., LEY, A. B. & LADUE, J. S. **Detection of Hepatitis Carriers by Serum Glutamic Oxalacetic Transaminase Activity.** *J. Amer. Med. Ass.* 1959, Dec. 26, v. 171, No. 17, 2303–6. [15 refs.]

No objective method exists whereby carriers of the virus of homologous serum hepatitis can be detected, and excluded as blood donors. Taking advantage of the observation that the activity of serum glutamic oxalacetic acid transaminase (SGO-T) increases early in serum-transmitted and infective hepatitis, the authors tried to correlate the activity of this transaminase in the blood of donors in New York with the incidence of jaundice in the recipients in the 6 months following transfusion. It was important that donor serum should be separated early from the cells, otherwise falsely high readings were obtained.

Of 4,240 recipients, a 6-month follow-up was achieved in 1,371. Of these, 603 had received blood with a normal SGO-T content, and the incidence of jaundice was 1·5%. 768 had received blood from a donor with a raised level of the enzyme, and 5·5% of these subjects developed jaundice; further analysis of the latter showed a significantly higher incidence of jaundice if the donor was one of the group with the highest enzyme levels.

Although they consider the SGO–T estimation to be the best objective measure of infectivity, the authors nevertheless do not recommend discarding donor blood if it shows increased transaminase activity.

Alan B. Raper

LEVY, D. **Poliomyelitis in Infancy and Childhood.** *Amer. J. Med. Sci.* 1959, Dec., v. 238, No. 6, 685–90.

An analysis of 1,489 cases of poliomyelitis in infants and children in Israel showed that (1) a biphasic onset was not typical in infancy and childhood, (2) meningeal irritation was less common in infancy than in later childhood, (3) in early infancy about one-fifth of the patients showed no pleocytosis in the cerebrospinal fluid, and (4) in both infancy and childhood about one-half of the patients had increased protein at the onset of the paralytic phase in the cerebrospinal fluid. These findings are all regarded by the authors as differing from standard text-book findings.

A. B. Christie

COLONNELLO, F. Possibilità e limiti della terapi cortisonica-ACTH nella poliomielite. [**Scope an Limitations of Cortisone-ACTH Therapy in Poli myelitis**] *Giorn. di Malattie Infettive e Parassi* 1959, Oct., v. 11, No. 10, 789–98, 6 figs. [16 refs Discussion 798–800.

In Brescia during 1957–58, 166 patients with acu poliomyelitis were given cortisone and corticotroph treatment. Intraspinal, intravenous and hypoderm routes have shown no advantage over oral dosag which is so much more convenient. Colonnello h reported on the first 39 cases of this series in a previo paper.

12 patients with the bulbar form of the disease we admitted in 1958. 6 of these were given prednison within a day or two of onset and they derived n benefit. All these 12 patients died.

In the present paper, Colonnello tabulates his resul in 121 cases in relation to the body segments whic the paralysis affected, namely, (a) abdomen and low limbs, (b) chest and upper limbs and (c) serious cas involving limbs, trunk and respiratory muscles. T results are classified into 6 groups—cure, very goo good, fair, no change and deterioration—and Colonnel explains what he implies by each term.

69 patients had pyrexia—99·5° to 104°F.—on admi sion and were given cortisone at once, 20 to 120 mgr daily according to age. Only 2 of these patien showed any extension of the paralysis after startin treatment; the others showed a most dramatic improv ment in what had been an ominous clinical picture the time of admission. 52 patients had no pyrexia their paralysis had recently set in and it did not spre after beginning the cortisone treatment.

Each course of treatment started with a cortiso preparation and continued with corticotrophin after time. 79 patients needed only one course of treatme of an aggregate dosage of 1–1·60 gm. In 42 others second course had to be given after an interval 10–15 days.

A cure was achieved in 35 patients, a very goo result in 50, a good result in 17, a fair improveme in 16 and there was no change in 3 patients. In n case was pain influenced by the cortisone-corticotr phin treatment, but Colonnella also claims that th hormone treatment allows the muscles affected to b submitted to passive and, in due course, active exe cises at an earlier stage. He is confident that th treatment saves the nerve cells from further dama in acute paralytic, other than bulbar, cases and sto extension of the paralysis. In the absence of a specif antibiotic drug against the virus, however, one mu guard against any exaggerated expectations.

The pathological anatomy of the poliomyelitis lesio is referred to: the point of damage or destruction nerve cells is surrounded by tissue which has unde gone congestive and oedematous changes and these m in their turn become exudative and destructive, wi extension of the paralyses, unless they are controll at the earliest possible stage. This points to th rationale of cortisone treatment. *J. Cauchi*

Terragna, A. La nostra esperienza sulla terapia della fase acuta della poliomielite con cortisonici. [**Our Experience in the Treatment of the Acute Stage of Poliomyelitis with Cortisones**] *Giorn. di Malattie Infettive e Parassit.* 1959, Oct., v. 11, No. 10, 809–22, 3 graphs. [31 refs.]

Terragna reports the results of cortisone treatment given to 98 patients, aged 1 month to 25 years, since 1957. The initial daily dosage was 7·5–50 mgm. of prednisone or prednisolone and 70–100 mgm. of cortisone and the doses were gradually reduced after the first few days. Courses of treatment lasted 8 to 22 days—with aggregate amounts of 50–400 mgm. prednisone, 115–600 mgm. prednisolone and 200–1,085 mgm. cortisone in each course. The synthetic derivatives of cortisone were mostly preferred because smaller doses were required to obtain the necessary degree of anti-inflammatory and anti-allergic action.

Clinically, 15 patients had monoplegia, 36 diplegia, generally symmetrical, 9 tetraplegia, 14 an ascending spinal lesion with signs of bulbar involvement; 19 showed polioencephalitis manifestations often with involvement of the muscles of deglutition and respiration and sometimes of all 4 limbs, 3 a facial paralysis only and 2 meningeal signs and symptoms without any localized paralysis. The diagnosis was confirmed in every case in the laboratory by virus culture and rise in titre of antibody.

The relevant particulars of each case are summarized in a useful table. 4 patients died the day after admission and the small quantity of hormone given them could not have affected the issue. In 4 other patients, with ascending paralysis, hormone treatment did not affect the course of the disease. In no case was the hormone treatment followed by extension of the paralysis or other aggravation of the condition. 69 patients had pyrexia and the fever subsided within the first 3 days of treatment. The cortisones relieved pain, permitted earlier mobilization of the affected muscles and reduced the risk of contractures developing during the acute stage. [Colonnello, on the other hand, found that cortisone treatment did not affect the pain.]

A year-old infant had been on prednisone treatment for asthmatic bronchitis for 12 days when she contracted a severe infection with poliomyelitis, which had broken out in the ward; she had bulbar involvement and this left her with various and serious functional disabilities: she was still alive 14 months later. In this case, which is outside the series of 98, it is believed that the prednisone treatment, which was already being given when the poliomyelitis supervened, averted a fatal outcome. *J. Cauchi*

Pejme, J., Werneman, H., Bergholtz, I. & Lennmarken, M. B. **A Five-Year Follow-Up of the Paralytic Poliomyelitis Cases occurring during the Stockholm Epidemic in 1953 including the Therapeutic Results in the Respirator Cases.** *Acta Med. Scandinavica.* 1959, Sept. 30, v. 165, No. 1, 25–8.

In the grave epidemic of poliomyelitis in Sweden in 1953 there were 633 paralytic cases in Stockholm alone. Follow-up reports were issued in 1956 and 1957. In this article the results are reported after 5 years.

Since the 1957 report an additional 8 persons have become "employable", bringing this category up to 396 persons (63%). In addition there are 33 housewives and 132 employees who are classified as "fit despite some disablement". The total of those capable of being employed, including the affected children, are now recorded as 561 (89%); the unemployable number 40 (6%) and the deaths 33 (5%).

The duration of respirator treatment among 89 patients was from a few days to 6 months in the vast majority; 5 cases required a respirator for 6 months to 3 years; and 9 cases still require a respirator after 5 years. Among 31 tracheotomy cases 14 had the tube removed in less than 1 month, and the remainder at varying times up to 10 months. *H. Stanley Banks*

MacLeod, D. R. E., Armstrong, C. W. J., Moss, G. W. O., Potter, F. C. & Wilson, R. J. **Poliovirus Antibody Response after Various Vaccination Schedules and at Different Ages.** *Canadian Med. Ass. J.* 1959, Sept. 15, v. 81, No. 6, 443–9, 5 figs. [16 refs.]

The response of infants, children and adults to Connaught Laboratories poliovaccine has been under investigation since 1955 [this *Bulletin*, 1957, v. 32, 1031]. In this paper the results are presented and analysed. (1) *Response of triple negatives of various ages.* The response did not vary significantly with age although there was a suggestion that infants responded less well. Thus, in infants under one year, 68, 100 and 84% responded to a primary course with antibodies to types 1, 2 and 3 respectively. Figures for children 6–14 were 82, 100 and 89% and for adults 87, 93 and 100%. After a booster dose all the infants and children showed a response to all 3 types of virus except that only 93% of the infants responded to type 1. The response of infants with and without maternal antibody measured 10 months after the primary course showed no interfering effect of passive antibodies. This is contrary to the findings of Perkins *et al.* [this *Bulletin*, 1958, v. 33, 1021, *ibid.*, 1959, v. 34, 735] but it is noted that the levels of passively acquired antibodies in the Canadian children were much lower than in the British ones, and that such an interfering effect was noted in a study of quadruple vaccine [see p. 466].

(2) *Effect of different dose schedules.* It was found that there was very little difference between the responses measured after a booster dose when 1, 2 or 3 doses were given as a primary course. However, the children that were given 3 doses had the first 2 at 1 week's interval and the third 3 weeks after the second. Most children receiving 2 doses had them at a 4 weeks' interval. The booster doses were given 10 months after the end of the primary course. The authors believe that a booster type of response begins to occur about 1 month after the primary course and continues to develop over the next months. They therefore believe that a course of vaccine should consist of 3 doses given with an interval of at least 4

weeks between them and preferably 6 weeks." They stress that it is important to give the whole series of inoculations before the next poliomyelitis season.

(3) *Duration of antibody level.* Blood samples were obtained from a group of children aged 8–9 years, who had been vaccinated originally in 1955, 18 months after their booster dose. In general, antibody levels had been well maintained and there was an average loss of about 2-fold. It is concluded that the problem of the maintenance of immunity against poliomyelitis by means of killed vaccine should not present any problems different from those faced with other killed antigens.

[This is an interesting paper which deserves to be read in full.] *A. J. Beale*

GELFAND, H. M.; LEBLANC, Dorothy R.; FOX, J. P.; POTASH, L. **Studies on the Development of Natural Immunity to Poliomyelitis in Louisiana. III. The Serologic Response to commercially produced "Salk Vaccine" of Children totally or partially susceptible to Poliovirus Infection** [GELFAND, LEBLANC, FOX & POTASH]. *Amer. J. Hyg.* 1959, Nov., v. 70, No. 3, 303–11, 1 fig. [20 refs.] **IV. Natural Infections with Polioviruses following Immunization with a Formalin-Inactivated Vaccine** [GELFAND, LEBLANC, POTASH & FOX]. *Ibid.*, 312–27, 1 fig. [12 refs.]

These 2 papers continue to record the results of important surveys of poliovirus and other enterovirus infections in a group of Louisiana families which are significantly increasing our knowledge of the natural history of these virus infections and the influence of immunization upon them [this *Bulletin*, 1958, v. 33, 931 *bis*; 1959, v. 34, 1231].

III. The first paper records the response of these well-studied individuals to killed poliovaccine. Since routine samples of faeces were obtained it was possible to remove individuals from analysis who had acquired a natural poliovirus infection during the course of killed vaccine immunization and in this way to exclude one of the possible sources of error in the usual studies of the response to killed poliovaccine. 369 people received a primary course of 2 inoculations of 1 ml. separated by 1 month. Nearly a year later a third dose of vaccine was administered. This vaccine was of especially high potency for animals because of the disappointing results that had been obtained with the primary vaccination. The response of 156 triple negative children who were not naturally infected during the study was poor, 28%, 12% and 50% failing to produce antibodies to a titre of 1/2 after a primary course of inoculation. After a third booster dose 14% for type 1, none for type 2 and 37% for type 3 still lacked antibodies as judged by results in 79 children. Similarly, the geometric mean titres were low, thus after 2 doses they were for type 1 : 1/4, type 2 : 1/8, type 3 : 1/2·5 and after 3 doses they were 1/43, 1/370 and 1/7 respectively. The presence of heterologous antibodies greatly improved the response, thus subjects with type 2 antibodies responded better to both type 1 and type 3 and, similarly, type 1 or 3 antibodies enhance the response to type 2. In the same way the possessio of antibodies to type 1 appeared to increase th response to type 3 but the response to type 1 was hard affected by the presence of type 3 antibodies. The cross-reactions may not only help the efficacy of kille vaccine but also indicate that some cross-protectio between the types may be possible. The authors su gest, therefore, that a type 2 living vaccine might b effective in combating an epidemic due to type 1 [*ibid.* 1959, v. 34, 835] or type 3. [This has, of course, bee tried by HALE and his colleagues in Singapore, *ibid.* 1959, v. 34, 991.]

IV. The frequency of poliovirus infections amon the Louisiana families in 1954 and 1955 were com pared with those in 1956 and 1957 when all th persons without antibodies had been given killed poli vaccine. The seasonal pattern of infection was simila in the 4 years but the most significant difference wa the decrease in the number of episodes of infection i 1957 when there were only 7 episodes as opposed t over 45 in all the previous years. Type 3 was th predominant virus in 1954 and type 1 in 1955 and 19 and type 2 infections occurred frequently in 1954 an 1955 but were very infrequent in 1956. It seemed supe ficially that the low rate of infection with poliovirus in 1957 could have been due to the use of the kille poliovaccine. However, detailed study revealed th this was not the case. The rate of infection of natural immune persons in all the years was between 17 an 21%, and for naturally susceptible persons, regardle of whether they had been immunized or not, 80–90%

Naturally immune people apparently excreted polio virus for shorter periods and the titre of the virus wa less than in vaccine immune or susceptible individuall The reason for the difference in response of the natural immune and the vaccine immune subjects is uncertai The authors note, however, that the titre of the va cine immune compared with the naturally immun persons was considerably lower. Similarly, there wa some suggestion that subjects who had had 3 doses o killed vaccine or who had a higher titre after 2 dos showed a slightly shorter duration of faecal excretio after natural infection with polioviruses. The autho note that the results of their survey do not support th idea advanced by SALK (*Modern Medicine*, 1958, v. 2 83) that oropharyngeal virus excretion may play a important role in virus spread. It has been shown tha oropharyngeal excretion is limited or abolished i individuals with high antibody levels and the fact tha in the Louisiana families infection still proceeds readil despite vaccination implies that oropharyngeal excretio does not play the major role in the spread of polio virus infections under the conditions studied. [Actua examinations of pharyngeal secretions are not re ported.] As a result of this study it is concluded tha the decline in episodes of poliovirus infection in 19 is due to a natural decline in the epidemic cycle fo poliovirus.

[These 2 important papers deserve to be rea in the original. The represent a final summary o the data already presented in a preliminary form b Gelfand *et al.*, this *Bulletin*, 1957, v. 32, 1031 an Fox *et al.*, *ibid.*, 1959, v. 34, 112.] *A. J. Beale*

Lennette, E. H., Magoffin, R. L., Schmidt, Nathalie J. & Hollister, A. C., Jr. **Viral Disease of the Central Nervous System. Influence of Poliomyelitis Vaccination on Etiology.** *J. Amer. Med. Ass.* 1959, Nov. 14, v. 171, No. 11, 1456–64, 1 fig. [19 refs.]

This valuable paper records the results of laboratory investigations of cases of suspected virus disease of the central nervous system occurring in California in the years 1955, 1956 and 1957. Extensive attempts at virus isolation were made by using monkey kidney cells and suckling mice. Also serological tests for polio, herpes simplex, mumps, Western equine and St. Louis encephalitis viruses were performed. In all 1,407 patients were studied, diagnosed clinically as paralytic poliomyelitis, non-paralytic poliomyelitis, aseptic meningitis or encephalitis.

The main object of the study was surveillance of poliovaccine safety and effectiveness. It was found that poliovirus isolations were less frequent from vaccinated individuals with a diagnosis of paralytic poliomyelitis or non-paralytic poliomyelitis and aseptic meningitis than in unvaccinated individuals. Similarly the isolation rate of other viruses was higher in vaccinated individuals and so was serological evidence of infection with agent other than poliovirus. Thus, for children under 4 with a diagnosis of paralytic poliomyelitis poliovirus was isolated from 81%, 77% and 36% in those with none, 1, or 2 or more doses of vaccine. 21 children had had 3 or more doses and only 1 yielded a poliovirus. The isolation of other enteroviruses rose with vaccination status, being 2%, 3% and 21% in those with 0, 1, or 2 or more doses. Similar findings occurred in the other age-groups and for aseptic meningitis (including non-paralytic poliomyelitis). Thus in children with aseptic meningitis aged 5–14, 22% and 20% respectively yielded a poliovirus and an enterovirus in the unvaccinated, whereas the figures were 3% and 40% for those who had had 2 or more doses. Similarly the severity of the poliomyelitis was greater in general among unvaccinated persons and those yielding poliovirus than in vaccinated persons not yielding poliovirus. There were 121 cases of encephalitis but only 2 patients yielded poliovirus and neither was vaccinated. [Table 3 of the paper records slightly different figures for encephalitis than the text.] The serological results confirmed the above disparity in incidence of poliovirus and other virus infection in vaccinated and non-vaccinated individuals, and support the conclusion that this disparity is strong evidence of high poliovaccine effectiveness.

The authors stress the difficulty of assigning an aetiological role to the Coxsackie and ECHO viruses isolated from paralytic cases, but are inclined to think they were the causative agent in some cases at least. They also note that the aetiology of much "viral" disease of the central nervous system remains to be determined.

[This is a most interesting paper which should be required for those interested in virus diseases of the central nervous system.

See also this *Bulletin*, 1958, v. 33, 440.]

A. J. Beale

Miraglia Del Giudice, M., Picciotto, L. & Pontecorvo, M. La vaccinazione antipoliomielitica delle gestanti. [**Poliomyelitis Vaccination in Pregnancy**] *Riv. Istituto Sieroterap. Ital.* 1959, Nov.–Dec., v. 34, No. 6, 482–92. [18 refs.]

The English summary appended to the paper is as follows:—

"572 pregnant women were given poliomyelitis vaccine (Salk type). The vaccine was administered in two doses given at one month intervals during the last trimester of pregnancy.

"The antibody response was investigated in a group of 27 women.

"Blood specimens taken before, during the course and at the end of vaccination (two weeks before delivery) were tested for neutralizing antibodies. The same assay was performed on infants bled at 21 days of age.

"Before vaccination all the mothers had naturally occurring antibodies. The first of two doses of vaccine appeared to produce a marked booster response. At the end of vaccination in all the subjects the antibody titers were substantially higher than the pre-existing ones. Infants born to tested mothers exhibited antibody levels correlated to the mother's titers.

"The utility of vaccine administration to pregnant women is emphasized as are discussed the implications concerning the local immune-epidemiological aspects."

Schweiz. Med. Woch. 1959, June 27, v. 89, No. 26, 671–702, numerous figs. [Numerous refs.] Poliomyelitisähnliche Krankheiten. Fortbildungstagung der Schweizerischen Vereinigung gegen die Poliomyelitis. Basel, 27./28. Februar 1959. [**Poliomyelitis-like Diseases. Seminar Session of the Swiss Union against Poliomyelitis. Basle. 27–28 February 1959.**]

At a session of the Swiss Union against Poliomyelitis held in Basle on 27–28 February 1959, 9 papers were read on the subject of virus diseases of the central nervous system resembling poliomyelitis. O. Gsell (*Serous meningitis and its causes*, pp. 671–674) describes the difficulties involved in making a provisional diagnosis of serous meningitis on the basis of clinical observations. The differential diagnosis of various types of serous meningitis, and between the latter and encephalomyelitis, is outlined in tables, and a case history is given to illustrate the fact that a great deal of work by specialized laboratories is required for the establishment of a diagnosis. In spite of these difficulties the percentage of cases in which the aetiology can be established has risen during the last 10 years, and amounted to 94% in a series of 63 cases reported in 1957 by Wiesmann and co-workers [this *Bulletin*, 1959, v. 34, 199]. The part played by the Coxsackie viruses in the causation of disease in man is reviewed by H. Löffler (*Coxsackie virus*, pp. 674–676), who found Coxsackie A in 1%, Coxsackie B in 4% and an ECHO virus in 50% of 63 strains isolated in Berne in 1958 from patients suffering from serous meningitis; one-third of the strains of ECHO virus were of type 9. The ECHO viruses are discussed further by U. Krech

(*The significance of the ECHO viruses in the aetiology of illnesses resembling poliomyelitis*, pp. 676–680). A laboratory infection with ECHO type 9 is described. Infectious material was accidentally sprayed on to the face of a laboratory worker; 30 minutes later 3 cc. of gamma globulin with a high content of ECHO 9 neutralizing antibody were injected intramuscularly, but 3 days later the typical illness developed, and the virus could be isolated from the blood, cerebrospinal fluid and throat swabs. Epidemics of ECHO virus infection have occurred in Switzerland in 1956, 1957 and 1958, with a seasonal incidence coinciding with that of poliomyelitis.

The importance of the myxoviruses is discussed by O. VIVELL (*The myxoviruses as causative agents of abacterial meningitis*, pp. 680–683).

Of particular interest is the contribution of H. MORITSCH (*Virus infections of the central nervous system transmitted by arthropods in Europe*, pp. 683–686). The disease originally described as Russian spring-summer encephalitis has been found in recent years to occur in various parts of Central Europe, and in its various clinical and epidemiological forms has now come to be known as tick-borne encephalitis. The disease has not yet been observed in Switzerland, and gamma globulin prepared from Swiss blood donors does not as yet contain any neutralizing antibody to the virus. In the area of Neunkirchen in Austria 89 of 162 cases (55%) of serous meningitis observed in 1956–58 could be shown to be due to infection with tick-borne encephalitis virus. The main incidence occurred between June and September. The virus is known to be transmitted by ticks and by the consumption of infected milk, but there is always a definite proportion of cases in which these routes of infection can be excluded.

In *Paretic diseases resembling poliomyelitis* (pp. 688–694) E. ROSSI, M. REUTSCH and U. KRECH survey the groups of viruses which can produce a paralytic illness, and give case histories illustrating paralysis caused by infection with Coxsackie A and B and ECHO 9 viruses. Further case histories and a discussion of the clinical aspects are given by A. HOTTINGER (*Demonstrations of poliomyelitis-like illness in childhood*, pp. 695–699).

M. SCHÄR (*The epidemiology of poliomyelitis in Switzerland in 1958*, pp. 699–701) points out that the usual seasonal increase in the incidence of poliomyelitis in Switzerland in the summer and autumn months did not occur in 1958. The incidence curve for this year coincided with that for 1945, and the reduced incidence cannot therefore be immediately ascribed to the successful use of poliomyelitis vaccine. The annual incidence since 1935 has varied in a cyclic manner, with minima in 1935, 1943, 1945 and 1950. The low incidence in Switzerland in 1958 was also paralleled in France and Germany, whereas summer-autumn epidemics of the usual type occurred in Italy and Aus ria.

A final paper by M. REUTSCH (*Poliomyelitis-like paralysis with a chondroma of the proximal tibial metaphysis*, pp. 701–702) presents the case history of a child aged 6 weeks who presented with apparent weakness and wasting of the left leg. Poliomyelitis was considered in the differential diagnosis, but on X-ra examination a chondroma of the proximal tibial meta physis was found, and when this was excised th symptoms disappeared. *D. J. Bauer*

WALKER, Selma J., MCNAUGHTON, G. A. & MCLEAN D. M. **Coxsackie B5 Virus Infections in Children Toronto, 1958.** *Canadian J. Pub. Health.* 1959 Nov., v. 50, No. 11, 461–7, 2 figs. [12 refs.]

This paper continues the series of reports of studie of abacterial meningitis and related viral diseases fro the Hospital for Sick Children in Toronto. It also contains a review of the results obtained in the pre vious 8 years. In 1958 specimens were examined fro 113 patients with clinical syndromes of abacterial menin gitis, pleurodynia, pericarditis, abdominal pain an paralytic poliomyelitis. 69 patients suffered fro abacterial meningitis and a virus was isolated from th stools of 62% and from the cerebrospinal fluid o 47·8% of those examined. The predominant virus wa Coxsackie B5 representing 33 out of the 43 isolate from stools. 5 strains of ECHO 9 virus were isolate and 1 each of the following—ECHO 6, Coxsackie A9 B3 and B4. 1 strain remains to be identified. 16 out o 18 cases of pleurodynia yielded Coxsackie B5 virus an 2 out of 5 tested from the cerebrospinal fluid. Simi larly, 5 out of 8 patients with pericarditis yielde Coxsackie B5 virus. 11 cases of abdominal pain wer investigated and Coxsackie B5 virus was isolated fro 5, Coxsackie B3 from 1 and an untyped virus from 1 6 cases of paralytic poliomyelitis were examined an 4 yielded a poliovirus, 2 type 1, 1 type 3 and 1 type 2 The 2 patients who had type 1 infection had had doses of killed poliovaccine. All the other patient were unvaccinated. There was also a patient with non paralytic poliomyelitis who was excreting type 2 polio virus but failed to develop any neutralizing antibodie to any of the types of poliovirus. The detailed result of all the patients complete with serological data ar presented in a series of tables.

The authors note that in the previous 8 years Cox sackie B5 virus had not been isolated in Toronto an they note that the clinical manifestations of Coxsacki B5 infection varied from abacterial meningitis to peri carditis and Bornholm disease. In view of the prob able rarity of Coxsackie B5 infection in the communit in the previous 8 years they believe that the presenc of high titres of Coxsackie B5 in the serum is highl suggestive evidence of Coxsackie B infection. Thus al the 18 patients with pleurodynia and the 8 with peri carditis had serological evidence of previous or curren Coxsackie B5 virus infection. *A. J. Beale*

PAFFENBARGER, R. S., Jr., BERG, G., CLARKE, N. A. STEVENSON, R. E., POOLER, Barbara G. & HYDE R. T. **Viruses and Illnesses in a Boys' Summe Camp.** *Amer. J. Hyg.* 1959, Nov., v. 70, No. 3 254–74, 6 figs. [17 refs.]

A survey of sickness and virus excretion (as detecte in monkey cells) in nasal and rectal swabs was mad at a boys' camp in Kentucky in the summer of 1957 During the summer 732 boys stayed at the camp wit

34 adult counsellors. 681 of the boys co-operated in the virus studies. Boys aged mainly 8–14 years lived 12–14 in each cabin but took part in communal activities, particularly swimming. 37 viruses were isolated—16 Coxsackie B4, 4 A9, 6 ECHO 14, 1 ECHO 1 and 5 unclassified ECHO viruses. 5 adenovirus, all except 1 (type 5) type 3, were also isolated. The only virus associated with clinical illness was Coxsackie B4. 7 of the 12 boys infected with this virus after entering the camp had febrile illness. By contrast there were 386 episodes of minor illness—mainly with respiratory or gastro-intestinal symptoms—among the boys. The main purpose of this enquiry was to estimate the relative importance of personal contact and indirect contact *via* play equipment and the swimming pool in spreading infection. It was found that so far as virus infections were concerned personal contact in cabins was by far the most important factor and that the swimming bath played no measurable part despite frequent inadequate chlorination. Similar findings were obtained with mild illnesses. However, respiratory symptoms appeared to spread not only in cabins but also at the swimming pool. The authors speculate that since the spread of poliovirus in families is much more widespread than that of enterovirus in cabin mates, the greater personal hygiene engendered by the swimming pool may be an important factor. In an addendum they suggest that an inert tracer substance might be used in a swimming pool to decide whether its role is as a reservoir of infection or as a cleansing station.

A. J. Beale

FOLEY, J. F. & CHIN, T. D. Y. **Outbreak of Non-bacterial Gastroenteritis at a Boy Scout Ranch.** *Pub. Health Rep.* Wash. 1959, Nov., v. 74, No. 11, 1015–23, 2 figs. [19 refs.]

This is an account of an outbreak of nausea, vomiting, and diarrhoea affecting 171 out of 1,457 staff and guests of a Boy Scout Camp in New Mexico during August 1957. The duration of the illness was a few hours to 3 days; more children than adults were affected, and multiple cases in families were common; no bacterial pathogens were isolated from the patients; transmission was by person to person contact; there was no evidence of an infected water, milk, or food supply. These features are characteristic of non-bacterial gastroenteritis, a condition which has mostly been described in institutional populations [this *Bulletin*, 1951, v. 26, 975]. Viral studies with suckling mice, tissue culture, and haemadsorption techniques were negative; the finding of a Coxsackie-like virus in 4 instances was almost certainly coincidental.

H. Stanley Banks

SOLOMON, P., WEINSTEIN, L., CHANG, Te-Wen, ARTENSTEIN, M. S. & AMBROSE, C. T. **Epidemiologic, Clinical, and Laboratory Features of an Epidemic of Type 9 ECHO Virus Meningitis.** *J. Pediatrics.* St. Louis. 1959, Nov., v. 55, No. 5, 609–19, 2 figs. [25 refs.]

This is an excellent account of a summer epidemic of virus meningitis with an accompanying maculopapular, occasionally petechial, rash on the face and trunk of a proportion of the patients, mostly in the children (in this instance in 28% of 64 cases described). This type of epidemic occurred in Great Britain in 1954 and 1955 [this *Bulletin*, 1957, v. 32, 556; 1958, v. 33, 317], was at first designated "Nottingham meningitis", but was quickly discovered to be associated with ECHO type 9 virus. In the summers of 1956 and 1957 similar outbreaks occurred in many countries of Europe, and also in Canada and the United States. This particular outbreak occurred in the summer of 1958 in the Boston area, and the report is based on the clinical and laboratory findings in 56 children and 8 adults. The ECHO 9 virus was proved to be the aetiological agent in 70% of the cases, and shown to be of probable significance in an additional 8%.

The following findings were different from those described in other similar outbreaks: (a) *severe* nuchal rigidity present only in 11%; though some neck stiffness was demonstrable in 70%, it was only slight or absent in as many as 61%; (b) abnormally high spinal fluid protein in 7 of the 8 adult patients; (c) absence of leucopenia, and frequency of leucocytosis with predominance of neutrophils. These features caused much difficulty in the differential diagnosis in one particular case between viral and bacterial meningitis. The latter was finally diagnosed on the basis of: (1) the marked nuchal rigidity, (2) a spinal fluid cell count of 2,500 per cmm. with 91% neutrophils, (3) spinal-fluid/blood sugar ratio falling as low as 19%. Any one of these findings alone is compatible with the presence of viral meningitis, but two or more should be highly suggestive of bacterial infection.

H. Stanley Banks

ELVIN-LEWIS, M. & MELNICK, J. L. **ECHO 11 Virus associated with Aseptic Meningitis.** *Proc. Soc. Exper. Biol. & Med.* 1959, Dec., v. 102, No. 3, 647–9.

In June and July 1958, 5 out of 7 cases of viral meningitis seen at the Jefferson Davis Hospital, Houston, Texas, came from a new low rental housing area. Rectal swabs were taken from members of 18 families in this area containing or having contact with a recent case of viral meningitis and from 18 families without such a history. The 18 control families lived in a slightly separate part of the housing development area and mixing of young children between the 2 groups of families was probably rare. 33 out of 74 specimens from the study families were infected with an enterovirus against 19 out of 83 controls. Families of the 5 children admitted to hospital yielded viruses as follows: 2 an ECHO 11 virus; 1 ECHO 4; 1 ECHO 4 and 11; and 1 ECHO 9 and poliovirus type 1 (in this instance the patient yielded ECHO 9 from faeces and cerebrospinal fluid). 19 out of the 33 viruses from the study group and 5 out of the 19 from controls were ECHO 11. Other viruses isolated from the study group were 7 ECHO 4, 1 each ECHO 6 and 9, 2 poliovirus 1, 3 poliovirus 3, and from the controls 3 ECHO 5, 4 ECHO 13, 2 each ECHO 15, Coxsackie B2 and B3, 1 ECHO B5.

Symptoms, usually those associated with viral meningitis, were present in 61% of the study group and

18% of controls. 12 out of 60 patients yielded ECHO 11 virus and 13 other enteroviruses. 27 of 97 symptomless individuals were carriers, and of these, 12 had ECHO 11 viruses. The results again illustrate the frequency of enterovirus infections with 1 virus usually predominant but with others also represented. They also illustrate the complexities of ascribing a specific role to enteroviruses in producing disease.

A. J. Beale

DOWNS, W. G. & ANDERSON, C. R. **Arthropod-Borne Encephalitic Viruses in the West Indies Area. Part I: A Serological Survey of Grenada, W.I.** *West Indian Med. J.* 1959, June, v. 8, No. 2, 101–9, 1 map.

The mountainous island of Grenada has a rainfall ranging from 50 inches per annum in the south-east to 160 in the hills. Dengue outbreaks are not recorded and 2 cases of yellow fever were last reported in 1901.

Sera were collected from areas representative of the different ecologies on the island. The strains of virus used were isolated either in Trinidad or Brazil. 179 sera were collected from 6 areas with representative numbers from both sexes in age-groups from 5 to over 50 years. No antibody to Mayaro virus was found. 2 coastal communities had incidences of 12% and 41% of neutralizing and 23% and 70% of haemagglutinin-inhibiting antibody to dengue virus (Tr 1751): very few sera from the inland communities had dengue antibody. Only 3 sera had neutralizing antibody to Ilheus virus although 11 others gave partial protection. Only sera giving partial protection against St. Louis encephalitis virus were found. One person aged 56 years had yellow fever neutralizing antibody. 38 sera with neutralizing or haemagglutinin-inhibiting antibody or both against one or more group B arborviruses were tested for complement-fixing antibody. Some with high haemagglutinin-inhibiting titres had no complement-fixing antibody, but many had high titres of both. Although dengue appears to have been responsible for most of the infections, higher complement-fixing titres were obtained with Ilheus and St. Louis viruses. The incidence of complement-fixing antibody suggests virus activity within 2 years of the survey (1956). The evidence suggests that only dengue, of the viruses used, is a common infection in Grenada.

C. E. Gordon Smith

i. JENKINS, A. A. & DONATH, R. **The 1958 Encephalitis Outbreak in Northern Utah. 1. Human Aspects.** *Mosquito News.* 1959, Dec., v. 19, No. 4, 221–2.

ii. THOMAS, L. A. & SMITH, J. V. **2. Infection Rates in Birds, Mammals, and Mosquitoes.** *Ibid.*, 223–6, 1 fig.

iii. REES, D. M., OGDEN, L. J., COLLETT, G. C. & GRAHAM, J. E. **3. Mosquito Populations in relation to the Outbreak.** *Ibid.*, 227–31, 3 figs.

i. There was an epidemic of encephalitis in Northern Utah in 1936, but not again until 1958. The first known case occurred in the middle of June and the peak of the outbreak was in the second week of August. The last known case was in late September. Sera from 48 patients were examined in the laboratory. 36 showed a 4-fold or greater increase in antibody titre against Western equine encephalitis virus. 11 had a high antibody titre in their convalescent sera and the virus was isolated from the brain of the only fatal case. 38 of the patients were male and 10 female. A serum survey was carried out in the area of the epidemic during the following November. 1 of 25 sera from infants had haemagglutinin-inhibiting antibody to western equine encephalitis virus, 13 of 145 school children had antibody and 3 of 27 adults.

ii. 7 of 80 pools of 3,741 *Culex tarsalis* collected from the area of the epidemic yielded western equine encephalitis virus. No isolations of St. Louis virus were made. The estimated incidence of infection in *Culex tarsalis* in different areas ranged from 0·09% to 0·7%. Western equine encephalitis virus was also isolated from the brain of a 2-month-old child. Sera from 32 close contacts of clinical encephalitis patients were tested and 3 had neutralizing antibody, but none of them complement-fixing antibody against western equine virus.

18 of 20 horse sera from the epidemic area had haemagglutinin-inhibiting antibody, 37 of 67 had complement-fixing antibody, and 62 of 71 had neutralizing antibody. Of sera from chickens less than one year old, 28 of 271 had haemagglutinin-inhibiting antibody and 8 of 50 neutralizing antibody. The incidence of antibody in chickens varied in different areas from 2% to 24%. These results suggest that inapparent human infections were uncommon, but infections in horses and chickens appear to have been very common during the epidemic.

iii. Larval collections of *Culex tarsalis* showed that there had been an increase in the number of pools containing larvae in 1958 of approximately 230% from 1957 and 440% from 1956. The increase was greatest during July and August. There was a slight increase in the number of pools containing *Aëdes dorsalis* and some increase also in those containing *Culiseta inornata* larvae. Light trap collections showed that the *Culex tarsalis* population was more than 4 times the average for the previous 2 years, but that there was no increase in *Aëdes dorsalis* or *Culiseta inornata.*

The average temperature for the first 9 months of 1958 was considerably above that of the same period for the previous 2 years. The mild winter and an earlier, warmer spring appears to have favoured high production of *Culex tarsalis.* Rainfall was higher during the first quarter and lower than normal during the third quarter in both 1957 and 1958. The average snow depth in April/June increased progressively from 1956 to 1958, meaning that there was abundant water supply for irrigation in 1958, which may have increased the production of *C. tarsalis.* *C. E. Gordon Smith*

BUESCHER, E. L.; SCHERER, W. F.; GROSSBERG, S. E.; CHANOCK, R. M.; PHILPOT, V. B., Jr.; KITAOKA, M.; OKUNO, T.; OGATA, T.; ROSENBERG, M. Z.; MCCLURE, H. E.; KUTTNER, L. J.; MOYER, J. T.; IZUMI, T. **Immunologic Studies of Japanese Encephalitis Virus in Japan. I. Antibody Responses following Overt Infection of Man** [BUESCHER, SCHERER, GROSSBERG, CHANOCK & PHILPOT]. *J. Immunology*. 1959, Dec., v. 83, No. 6, 582–93, 2 figs. [21 refs.] **II. Antibody Responses following Inapparent Human Infection** [SCHERER, KITAOKA, GROSSBERG, OKUNO, OGATA & CHANOCK]. *Ibid.*, 594–604, 3 figs. [12 refs.] **III. Infection and Antibody Responses of Birds** [BUESCHER, SCHERER, ROSENBERG & MCCLURE]. *Ibid.*, 605–13, 1 fig. [14 refs.] **IV. Maternal Antibody in Birds** [BUESCHER, SCHERER, ROSENBERG, KUTNER & MCCLURE]. *Ibid.*, 614–19. [16 refs.] **V. Maternal Antibodies, Antibody Responses and Viremia following Infection of Swine** [SCHERER, MOYER & IZUMI]. *Ibid.*, 620–26, 1 fig. [12 refs.]

I. American and Japanese patients in Japan in the summers of 1953, 1955, 1956 with clinical diagnoses of encephalitis, abacterial meningitis or poliomyelitis were studied. Serological studies on 127 patients yielded 84 "confirmed cases (4-fold or more increase in complement-fixing (CF) or haemagglutinin-inhibiting (HI) antibody or an increase in neutralizing (N) antibody from an index of <10 to >100) and 15 "presumptive" cases (sustained CF titre >16 or HI >80). Of 20 clinical cases confirmed by CF or HI or both a significant increase in N antibody was demonstrated only in 1; 7 of 8 patients bled within 4 days of onset and all of 9 bled between 5 and 8 days after onset already had N indices of 50 or more, so that increases could not be detected. 5 patterns of CF and HI antibody response were observed: (i) 49 patients had significant increases of both; (ii) 8 had an increase in HI antibody, but although CF antibody was present it did not increase; (iii) 5 had no CF antibody at any time, but HI antibody increased; (iv) 22 had unchanging high levels of HI antibody and significant increases in CF antibody; (v) 15 had both types of antibody without change. The CF antibody changes lagged behind HI changes: 30% of patients had CF antibody by the 8th day of disease compared with 75% with HI antibody; the maximum incidence of CF antibody was not reached until the 4th or 5th week while most patients had HI antibody by the end of the 2nd week. Diagnosis by CF was sometimes, therefore, possible with later serum samples rather than by HI. Higher CF and HI antibody titres were significantly more frequent among 64 American than among 20 Japanese patients.

Serum was obtained in 1955 from 26 servicemen who had had Japanese encephalitis in Korea in 1950: 19 had been "confirmed" and 7 "presumptive" diagnoses. All had significant N antibody which differed in level little from that of serum 60 days after the onset of disease 5 years earlier. Only 6 had CF antibody compared with 23 in 1950 and titres were markedly lower. 23 had HI antibody, but titres were 4–8-fold lower than in 1950. 4 of the 6 patients with persisting CF antibody were not known to have been exposed to possible group B arborvirus infection in the interim.

In diagnosis the neutralization test is often ineffective because antibody appears so early—however, the absence of N antibody 2 weeks after onset excludes the diagnosis. Both CF and HI tests should be used: 83–90% of patients showed a CF increase and about 75% an HI increase.

II. In 1956, 404 Japanese schoolchildren were tested monthly for antibody between June and November. Heparinized plasma was used and presented no serological difficulties. 14 children with no antibody at the beginning showed typical primary antibody responses, but responses were also detected in 7 children with pre-existing antibody. All were due to inapparent infections (with 1 possible exception). In the first group 13 of 14 developed N antibody, 11 CF antibody and all of them HI antibody. All 7 in the second group had N antibody in June, 1 had HI and none CF antibody: all had 4-fold or greater increases in CF and HI antibody. Evidence is presented that the neutralizing substance detected in June was in fact, antibody. The maximal titres of HI antibody in inapparent infections (10–320) were lower than those following clinical disease (80–5,120).

Of 64 children aged 6–12 years with N antibody as evidence of past inapparent infection, only 2 had CF antibody, while of 112 similar children 64 (55%) had HI antibody.

After inapparent infections with Japanese encephalitis, HI antibody appears more consistently than CF antibody; HI and N antibody often appear together but either may precede the other. Children with evidence of previous infection with Japanese encephalitis showed secondary serological responses apparently indicating natural infections in the face of circulating antibody. HI antibody does not persist as long as N antibody, thus the neutralization test must be used for surveys of past infections.

III. Following inoculation of 1–320 mouse LD50 of low passage strains of Japanese encephalitis virus, 8 of 17 wild birds (of 4 species) and 54 of 68 Leghorn chicks 3–10 days old had viraemia usually on the 2nd and 3rd day and lasting 1–5 days. No essential difference was found in the pattern in the wild birds and chicks. In 4 of 5 chicks given 19 LD50 viraemia rose to a maximum of 2·1–3·3 log between the 3rd and 5th day; in the 5th chick viraemia was not detected, but all 5 developed HI antibody. In chicks given $1{\cdot}9 \times 10^6$ LD50 all had viraemia from the first day lasting 3–5 days with maximum titres of 1·3–4·0 log. No difference was found between 6 strains of virus of human, mosquito and avian origin in their circulation characteristics. In 12 chicks given 1–10 million LD50, all had viraemia on the first and second days and none after the 5th day; all had HI antibody by the 7th day. In 13 chicks given 10–100 LD50 the majority did not have viraemia till the 3rd and 4th days and 2 still had viraemia on the 7th day; only 60% had HI antibody at the 5th day and 100% only after 14 days A small dose of 7th mouse passage virus caused viraemia

and an antibody response in all chicks while similar doses of 19th and 70–80th mouse passage virus infected only 2 of 7 and 2 of 6 respectively. Black crowned night herons (*Nycticorax nycticorax*) appeared to be more susceptible to infection than little egrets (*Egretta garzetta*). When chicks of different ages were given about 25 LD50 per ounce body weight viraemia and antibody responses were obtained in all at 2 weeks and about half at 6 weeks. Only 1 of 14 aged 3–14 months circulated virus, but about half showed antibody responses. CF antibody was never detected within 42–60 days after viraemia. HI antibody appeared within 2–3 days of the end of viraemia and reached maximum titres within 14–21 days. N antibody appeared 3–12 weeks after infection, but some birds with HI antibody had no N antibody 3 months after infection. The HI test, therefore, appears best for studies of Japanese encephalitis infections in birds.

IV. 5–10% of chicks aged under 2 weeks of age late in 1951 were found refractory to infection and were found to have neutralizing substances in their plasma before inoculation. 47 of 58 of the progeny of 6 hens experimentally infected with Japanese encephalitis 5 months before, were found to have N antibody 2 days after hatching. The incidence remained high until 7 days after hatching and fell into zero after 7 weeks. 1 of the 6 hens, although she had a similar titre of N antibody to the others, produced 9 of 16 progeny without antibody while all the progeny of the other 5 had antibody. About 50% of adult Japanese cormorants (*Phalacrocorax carbo hanedae*) have antibody [this *Bulletin*, 1958, v. 33, 443] and nestlings were collected before the Japanese encephalitis season: 5 of 16 nestlings aged less than 7 days had N antibody. 13 of 19 nestling herons and 7 of 15 nestling little egrets had N antibody and the titres in serial plasmas decreased from 2·0 to 3·5 log at 2 to 10 days to less than 1·0 at 25 days of age. Low HI titres (10) only were found in 2 of 6 herons. In a study of 26 herons and 37 plumed egrets (*Egretta intermedia*) 50% lost their maternal antibody by the 13–15th day (herons) or by 5–8 days (plumed egrets). More than 75% had lost their maternal antibody 21–30 days after hatching. 13 chicks with maternal N antibody were found to resist infection with 1,500 LD50 of Japanese encephalitis, but to be fully susceptible to infection with western equine encephalitis. Naturally occurring maternal antibody in herons was also found to protect against Japanese encephalitis infections. One heron, however, had viraemia after inoculation of 67 LD50 in spite of 3·0 log of N antibody. This may represent antibody to some other group B arborvirus acquired by the mother bird on her migration to south-east Asia. Once maternal N antibody had disappeared all birds were found to be fully susceptible to infection.

V. 68 of 80 pigs aged 2–7 months from farms near Tokyo were found to have N antibody in May; 12 had HI, but none of 73 had CF antibody. Antibody was commoner in pigs aged 2–3 months than in pigs aged 5 months or over. The antibody had disappeared in some of the pigs tested 2 months later. Because of this and because the Japanese encephalitis season has not started in May, these were apparently maternal antibodies. Maternal antibody disappears more rapidly in some pigs than others, the period varying from 1 to more than 3 months. Natural infections were studied in 6 pigs which had completely lost their maternal antibody before infection: only 11 developed CF antibody within 45 days of infection, whereas all developed HI antibody and all but 1 N antibody in the same period.

In 9 pigs naturally infected in mosquito traps HI antibody was sometimes found to precede N antibody: 1 of these pigs had viraemia in presence of HI (titre 10) and N (titre 1·8 log) antibodies. All of 4 pigs inoculated experimentally had HI antibody by the 7th day and 3 of them N antibody; only 2 had CF antibody by the 35th day. Viraemia was detected in 3 of 9 pigs naturally infected. 4 3-month-old pigs were inoculated with 10 to 32×10^6 LD50. Viraemia lasted 3–4 days starting on the day after inoculation with the highest doses, and on the 3rd day with the lowest. The maximum titres were 2·5–2·6 log.

C. E. Gordon Smith

SCHERER, W. F. & SMITH, R. P. J. ***In vitro* Studies on the Sites of Japanese Encephalitis Virus Multiplication in the Heron, an Important Natural Host in Japan.** *Amer. J. Trop. Med. & Hyg.* 1960, Jan., v. 9, No. 1, 50–55. [16 refs.]

VON ZEIPEL, G., SVEDMYR, A. & ZETTERBERG, B. **The Geographical Distribution in Sweden of Viruses belonging to the Russian Spring-Summer-Louping Ill Group. I. Serological Survey of Antibodies in Cow Sera.** *Arch. f.d. gesamte Virusforschung* 1959, v. 9, No. 4, 449–59, 4 figs.

A survey of cow sera was made because they are known to develop neutralizing antibodies after inapparent infections with Russian-spring-summer louping ill group viruses and are commonly bitten by the tick *Ixodes ricinus*. 2,780 sera were obtained from 5 abattoirs throughout the whole of the cattle-breeding area of Sweden. They were tested in Detroit-6 cells against 300 TCD50 of louping ill virus. 322 of 2,771 were positive. The incidence of positive sera increased markedly in the south-east compared with the rest of the area surveyed and this fits with the distribution of tick population. In the most heavily infected eastern region the incidence of antibody rose from 17% in cattle aged 1 year to 41% in cattle aged 2–6 years but only to 52% in cattle aged over 11 years. Young cattle are generally pastured out-of-doors day and night in the grazing season, while milking cows are generally indoors overnight. The former are more often pastured on natural pastures with scrub while the latter are more often on arable land. In the same region 44% of the cattle on pastures with scrub had antibodies compared with 26% of those on arable land—this closely paralleled the reported incidence of tick infestation of cows. The incidence of antibodies was compared with the incidence of piroplasmosis which is also tick-borne and a similar distribution was found.

C. E. Gordon Smith

VON ZEIPEL, G. **Isolation of Viruses of the Russian Spring-Summer Encephalitis-Louping Ill Group from Swedish Ticks and from a Human Case of Meningoencephalitis.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 4, 460–69.

898 starving adult ticks, probably all *Ixodes ricinus*, were collected in August–September from cattle on farms 60 miles north-east of Stockholm. 25 larvae and 35 nymphal ticks were also collected. Viruses were isolated from 3 of 23 pools of adult ticks and from the pool of nymphs. In 2-week-old mice the incubation period was less than 8 days. Blind passages on the remainder failed to demonstrate virus. On the positive pools titres in mice were from 2·4–4·5 LD50 per ml. In Detroit-6 cells apart from initial toxic effects, cytopathic changes were not seen until after 3 passages at 7–11 days and even after 10 passages the cytopathic effect was markedly less than with laboratory strains of Russian spring-summer (HYPR) and louping ill viruses. Cross complement-fixation and neutralization tests showed that the new isolates closely resembled HYPR and louping ill viruses.

Acute-phase sera from 26 patients with central nervous system disease and at least a 4-fold increase in complement-fixing antibody to HYPR virus were inoculated into Detroit-6 cells and no cytopathic effect seen. One of 22 sera inoculated into 2-day-old mice yielded a virus closely related to HYPR and louping ill viruses. 14 cerebrospinal fluids from these patients were inoculated into Detroit-6 cells and 2-day-old mice, but no virus was isolated.

[See also this *Bulletin*, 1959, v. 34, 609.]

C. E. Gordon Smith

ROSICKÝ, B. **Notes on the Classification of Natural Foci of Tick-Borne Encephalitis in Central and South-East Europe.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 4, 431–43, 1 fig. [37 refs.]

In tick-borne encephalitis the criteria for classification of natural foci of the disease are the tick vectors. In central and south-eastern Europe 3 types of infestation occur: wild infested areas, infested pastures, and mixed areas. Game preserves have very large tick populations. With forest clearance where there are no shrubs or uncontrolled pastures conditions are unsuitable for maintenance of ticks. Where shrubs and neglected pastures occur ticks may be numerous. 4 types of natural focus are described: (1) Theriodic foci (*theriodes*, Greek = wild)—forest sites with game preserves where large numbers of *Ixodes ricinus* are maintained on small mammals and birds. In one such focus in Bohemia 150 imagos and 3,600 nymphs were collected in 100 square metres in 1 year. These foci included vegetation types varying from low-lying riverside forests to mountain forests, and hornbeam (*Carpinus betulus*) and lime (*Tilia cordata*) are important indicators of suitable conditions. Man is infected in these areas when he enters forest for berry picking, picnics or woodcutting. (2) Bosquematic foci (*boskema*, Greek = domesticated)—forest pastures or pastures interspersed with thickets. Grazing animals are the principal maintenance hosts of *I. ricinus*. Man becomes infected either by tick bite while tending the animals or mowing grass, or through drinking infected raw goats' milk. Epidemics and family outbreaks occur in these foci compared with sporadic infections in theriodic foci. (3) Mixed theriodic-bosquematic foci. In such an area in Slovakia 60% of cases were due to tick-bite and 23% to drinking milk. Tick-bites were acquired—27% by attending grazing cattle, 22% by berry picking, 20% by collecting hay or wood, 16% in forestry and 2% in holiday-making. (4) Mountain foci. *I. ricinus* is almost absent and other vectors must maintain infection in small mammals. Human infections are rare.

C. E. Gordon Smith

BÁRDOS, V., ROSICKÝ, B. & VESENJAK-ZMIJANAC, J. **Notes on a Study of the Ecology of the Virus of Tick-Borne Encephalitis in the Slovenian Alps (Yugoslavia).** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 2, 162–7. [21 refs.]

Tick-borne encephalitis was first diagnosed in the Slovenian Alps in 1953 [this *Bulletin*, 1955, v. 30, 952] and these investigations were made to determine the animal reservoirs. Small mammals were trapped on the sides of a valley from 1,000 to 4,500 feet above sea level. 3–5 brains from the same species were pooled, ground and inoculated intracerebrally into mice. 3 blind passages were made. No isolations were made from 75 pools containing 188 brains. Neutralization tests with strain "O" virus were made on pools of heart-washings from the animals. The hearts were cut up in saline and allowed to stand overnight at 4°C. 30% of 62 pools had neutralizing antibody: the neutralizing indices were 1 pool with 50–90, 10 pools with 100–999, 8 pools with 1,000–9,999. Antibodies were found in almost all species examined and at all altitudes up to 3,000 feet. 10 of 16 specimens caught in the middle of the valley had neutralizing antibody and other positive animals were found in close association with human habitations. Neutralizing antibodies were found in 4 of 11 pools of *Sorex araneus*, 1 of 2 pools of *S. minutus*, 1 of 6 pools of *S. alpinus*, 3 of 5 pools of *Neomys fodiens*, 3 of 12 pools of *Apodemus flavicollis*, 2 of 12 pools of *Clethrionomys glareolus*, and 5 of 12 pools of *Pitymys multiplex*. Antibody has not previously been recorded in *P. multiplex*. The absence of virus isolations is probably explained because collections were made in June and July, the optimum months for virus isolation being April and May.

C. E. Gordon Smith

BLASKOVIC, D. **Note on the Problem of the Prevention of Tick-Borne Encephalitis.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1959, v. 3, No. 2, 132–7. [Numerous refs.]

Tick-borne encephalitis occurs in Sweden, in Finland, and in the whole of central, eastern and south-eastern Europe. Infections occur either through tick-bite or through ingestion of milk and milk products from infected domestic animals. Vaccination has been used especially for forestry workers in some foci of the

disease in Russia. As the vaccine is prepared from mouse brain the possible risk of allergic encephalomyelitis means that it is unsuitable for very large scale mass vaccination. Ticks may be controlled with insecticides either on a large scale by aerial spraying or by treatment of domestic animals. Improved care of pasture and surrounding scrub and forest can reduce the infestation of domestic animals. The incidence of neutralizing antibody in wild and domestic hosts of the ticks is probably important as when an infected tick feeds on immune blood its infection may be reduced in titre or completely neutralized. Vaccination of domestic animals is therefore suggested to reduce milk-borne infection and to diminish tick transmission in and around pastures. Young domestic animals could be immunized with live virus before their first lactation. Various new vaccines could be conveniently compared in trials in domestic animals. *C. E. Gordon Smith*

Gorchakovskaia, N. N. & Preobrazhenskaia, N. K. **The Reaction of *Ixodes persulcatus* and other Ticks to Treatment of the Forest Floor with DDT Dust in Foci of Tick-Borne Encephalitis.** *Problems of Virology.* London. 1958, v. 3, Nos. 5/6, 289–94. [Translated from Russian.]

"(1) Treatment of the forest floor with DDT dust at a rate of 0·3–0·4 g of a commercial preparation per square metre caused the death of 99·7 per cent of active adult ticks of the species *Ixodes persulcatus*, which are epidemiologically dangerous in a natural focus of tick-borne encephalitis.

"(2) In the spring and summer of 1955 the main hosts of larvae and nymphs in the district studied were bank voles, chipmunks and common hamsters.

"(3) Treatment of the forest with DDT dust considerably lowered the numbers of larvae and nymphs of *I. persulcatus* among voles (by 97·6 per cent). The number of tick-infested voles in the treated areas was decreased by 10·7 times.

"(4) Treatment of the forest with DDT dust may lead to a decrease in the number of certain blood-sucking gamasid ticks in the first season. In our experiments there was a decrease in the numbers of *Hirstionyssus eversmanni* in treated areas."

Iyer, C. G. S., Rao, R. L., Work, T. H. & Murthy, D. P. N. **Kyasanur Forest Disease VI. Pathological Findings in Three Fatal Human Cases of Kyasanur Forest Disease.** *Indian J. Med. Sci.* 1959, Dec., v. 13, No. 12, 1011–22, 10 figs. on 2 pls. [15 refs.]

The clinical features and pathology of 3 fatal cases of Kyasanur Forest disease [this *Bulletin*, 1959, v. 34, 203] are described in detail. Fever, aches and pains, toxaemia and haemorrhagic manifestations were the principal features. Haemorrhages occurred as petechiae in the skin, in the lungs giving signs of consolidation, and in the body cavities, viscera and gastro-intestinal tract. The main pathological features were parenchymal degeneration in the liver and kidneys, massive or patchy haemorrhagic pneumonitis and increased prominence of reticulo-endothelial tissue in the liv and spleen, with marked erythrophagocytosis. T virus was isolated from blood, liver, spleen, kidn lung, heart and skeletal muscle. Virus was not isolat from the brains and no evidence of encephalitis w found. One case showed prominent protoplasmic ast cytes in the brain and another prominent satellosis. a discussion of the pathogenesis, Kyasanur For disease is compared with the other haemorrha diseases caused or presumably caused by viruses. T authors believe that suppression of maturation in t bone marrow rather than lesions of capillary vess may account for the haemorrhagic manifestatio [Unfortunately the bone marrow was not examined the cases reported.] Leucopenia and thrombocytoper have been demonstrated. *C. E. Gordon Smith*

Govil, K. K., Bhadury, T., Gupta, N. P., Bajpai, P. Paul, S., Chakravarty, N. C. & Srivastav H. M. L. **Epidemiological Aspects of 1958-Ou break of Encephalitis in Lucknow.** *J. Indi Med. Ass.* 1959, Oct. 16, v. 33, No. 8, 320–2 [22 refs.]

An epidemic of encephalitis broke out in Luckno in the first week of July, 1958. 167 of a total of 3 patients admitted to hospital in July and August we investigated. Most had a sudden onset with high fev and the illness lasted 1–5 days. 166 had some loss consciousness, 110 having deep coma. 52% had cc vulsions, 61% had neck stiffness and Kernig's sig Polymorphonuclear leucocytosis and lowered sugar blood and cerebrospinal fluid were common. Few h increased cells in the cerebrospinal fluid. Tests of cc valescent sera for arborvirus antibodies were negati [The viruses used are not specified.]

There was no relation between population density different parts of the city and the number of patien admitted to hospital from them. The incidence start to drop in the last week of July and had almc finished by the end of August. More than half t patients were aged 2–5 years and 99% were aged und 13 years. No differences attributable to sex or religi were detected. More cases occurred in lower incor groups [but it is not shown what the distribution these groups in the population is]. 31 of 167 patie died, most of them aged 2–8 years. 165 were sing cases in a family, 2 families had 2 cases. In mc cases overcrowding and poor sanitation were found the houses. Association with domestic animals w common. Malnutrition was frequent. House flies we very common; mosquitoes and other blood-sucki insects were present in smaller numbers.

C. E. Gordon Smith

Scott, G. R. & Heisch, R. B. **Rift Valley Fever an Rift Valley Rodents.** *East African Med. J.* 19 Dec., v. 36, No. 12, 665–7.

"Neither Rift Valley fever virus nor Rift Vall fever antibodies were detected in the sera of 285 roden trapped in the Rift Valley of Kenya."

BLACK, F. L. **Measles Antibodies in the Population of New Haven, Connecticut.** *J. Immunology.* 1959, July, v. 83, No. 1, 74–82, 6 figs. [15 refs.]

An investigation has been made of the relationship between the occurrence of cases of measles in New Haven, Connecticut, and the development of immunity among the population. Outbreaks of the disease occur every 2–4 years and children aged 6 years are mainly affected. In an examination of 300 sera by neutralization and complement-fixation tests antibody was usually not present in children of pre-school age, but was found in 90% of sera by the age of 8–9. In 96 sera from children who had had measles up to 15 years previously there was no correlation between antibody titre and the time elapsed since the illness. There was also no correlation between titre and socio-economic class, but neutralizing antibody was found more frequently in children from families of 3 or more.

D. J. Bauer

GRAYSTON, J. T. & WATTEN, R. H. **Epidemic Rubella in Taiwan, 1957–1958. III. Gamma Globulin in the Prevention of Rubella.** *New England J. of Med.* 1959, Dec. 3, v. 261, No. 23, 1145–50, 1 fig. [10 refs.]

During a large island-wide epidemic of rubella in Taiwan in 1957–1958, controlled studies on gamma globulin as a prophylactic were carried out on some 500 boys in each of 2 primary schools, in which the epidemic reached its height 1 and 3 weeks respectively after the start of the experiment. In both schools 4 groups, each of approximately 100 boys, received either: (1) 5 ml. gamma globulin, or (2) 2 ml. convalescent gamma globulin, or (3) a placebo, or (4) no prophylactic treatment. The results showed that 5 ml. gamma globulin appeared to reduce the incidence of rubella by 70% (when cases occurring during the first week after inoculation were excluded). The boys who received 2 ml. convalescent gamma globulin (which had been in store for 6 years) had an attack rate similar to that in the placebo and uninoculated control groups. The period of partial protection from rubella extended from 1 to 12 weeks after the inoculation.

It is considered that this evidence considerably strengthens the case for prophylaxis of rubella with gamma globulin during an epidemic—a case which hitherto has rested on somewhat insecure foundations. In addition it was observed that the boys who received gamma globulin and who none the less contracted rubella, did not have any modified attack of the illness.

H. Stanley Banks

KLIJN, L. C. Heroriëntatie ten aanzien van enige problemen betreffende mononucleosis infectiosa. [**Re-Orientation in Respect of Some Problems relating to Infectious Mononucleosis**] *Nederl. Tijdschr. v. Geneesk.* 1960, Feb. 13, v. 104, No. 7, 327–32. [33 refs.]

The English summary appended to the paper is as follows:—

"The epidemiology, aetiology and clinical manifestations of infectious mononucleosis (SPRUNT and EVANS) have been investigated. The relationship between this disease and PFEIFFER's glandular fever has also been evaluated. A positive result to the indirect Paul-Bunnell test (with blood serum absorbed by a suspension of guinea pig kidney) is essential for the diagnosis of infectious mononucleosis.

"The clinical picture is monomorphic. Complications are rare. Infectious mononucleosis should be considered a sporadic-endemic disease. The evidence for the identification of infectious mononucleosis with PFEIFFER's glandular fever is inconclusive; the arguments for differentiation are more convincing. As the aetiology of the disease is as yet unknown, the above conclusions must for the time being remain hypothetical."

DOUGLAS, W. A. C. **Infectious Mononucleosis with Thrombocytopenic Purpura in a Child.** *Med. J. Australia.* 1959, Oct. 17, v. 2, No. 16, 564–6, 5 figs.

Within the last 10 years there have been a few reports of a rare complication of glandular fever—thrombocytopenic purpura (ANGLE and ALT, *Blood*, 1950, v. 5, 449; OGILVIE and PARRY [this *Bulletin*, 1953, v. 28, 319]). This is a further and well documented case in a child of 7. The boy was admitted to hospital in Brisbane because of a petechial rash and sore throat. He was found to have enlarged glands and liver and spleen, haemorrhagic tonsils, and petechiae on the lips, face, ear, neck and trunk, and bruises on the legs; his blood picture showed 20% atypical monocytes, and a marked thrombocytopenia (8,000 platelets/cmm.). The Paul Bunnell test after absorption was positive. On the day after admission the platelets fell to 1 per 100 oil fields, and Hess's capillary fragility test was positive and the bleeding time greater than 20 minutes. On the 3rd day the haemorrhage increased in the tonsils and skin, and therapy with corticotrophin 20 units crystalline and 20 units gel preparation, was started intramuscularly. 2 days later the petechiae were fading, the platelet count was 1,500/cmm. and the bleeding time 8 minutes. Clinical and haematological improvement continued and the boy was discharged with a normal platelet count 13 days after admission.

[This rare complication seems to be self limited, and although improvement was rapid after corticotrophin therapy, in this case the improvement might have been spontaneous.] *H. Stanley Banks*

ERWIN, W., WEBER, R. W. & MANNING, R. T. **Complications of Infectious Mononucleosis.** *Amer. J. Med. Sci.* 1959, Dec., v. 238, No. 6, 699–712, 4 figs. [68 refs.]

This article includes 5 detailed clinical reports followed by a discussion of the complications of the disease under the headings of neurological, ocular, pulmonary, renal, cutaneous, abdominal, hepatic, haematological and cardiac. These are discussed in some detail, with references to the literature, and the article can be recommended as a valuable review of the subject.

A. B. Christie

DODD, M. C., GRABER, C. D. & ANDERSON, G. **Hemagglutination of Rabbit Erythrocytes by Pus from Cases of Cat Scratch Fever.** *Proc. Soc. Exper. Biol. & Med.* 1959, Dec., v. 102, No. 3, 556–8.

"Hemagglutination of rabbit red cells with pus obtained from lymph nodes of 10 cases of cat scratch fever was demonstrated. Specificity of hemagglutinin was indicated by inhibition by serum from a known case of the disease and by rabbit antiserum to the pus."

KLUGE, R. C., WICKSMAN, R. S. & WELLER, T. H. **Cytomegalic Inclusion Disease of the Newborn. Report of Case with Persistent Viruria.** *Pediatrics.* Springfield, Ill. 1960, Jan., v. 25, No. 1, 35–9.

"Clinical and virologic studies are reported of a patient with neonatal cytomegalic inclusion disease. Jaundice, purpura and hepatosplenomegaly were noted shortly after birth and thereafter the course during a 2-year follow-up period was primarily one of impovement. At the end of this period signs suggestive of developmental difficulty were present as evidenced by impairment of speech and a head circumference below the 3rd percentile for age.

"Cytomegalic virus was recovered from the urine at 2 and 5 weeks and at 3, 16, 21, and 26 months of age, suggesting that viruria was a constant feature during the period of observation. Neutralizing antibody for the virus was present in the patient's serum during the period of viruria. Recovery of cytomegalic virus from the urine during the neonatal period would appear to be a useful diagnostic procedure. However, the demonstration of viruria in the older infant does not necessarily have the same diagnostic significance."

NELSON, Ethel R. **Hemorrhagic Fever in Children in Thailand. Report of 69 Cases.** *J. Pediatrics.* St. Louis. 1960, Jan., v. 56, No. 1, 101–8, 5 figs.

Sporadic cases of haemorrhagic fever had been seen in Thailand before 1958, when there was an epidemic. This is a study of 69 patients during 1958.

All had fever varying from 101 to 105°F. lasting 1–2 weeks. 40% had cough and pharyngitis, and dyspnoea and cyanosis occurred in severely ill patients with broncho-pneumonia and pleural effusion. 60% had abnormal chest X-Rays. 70% had nausea and vomiting, 21% anorexia, 25% abdominal pain, 13% diarrhoea and 25% constipation. 45% had enlarged livers. All had bleeding tendencies, most often a petechial rash or ecchymoses at injection sites. 22% had haematemesis, 15% melaena and 10% epistaxis. A few had maculopapular rash; headache or signs of meningeal irritation were seen in most severe cases.

There were 16 deaths, 14 of them within 48 hours of admission to hospital. 5 of 13 infants under 1 year of age died. 19% had haemoconcentration. The leucocyte count was normal in 53%, increased in 38% and 9% had leucopenia. 65% of 62 patients had thrombocytopenia of less than 100,000 per cmm. The platelet count increased very rapidly with improvement of the patient. Slight albuminuria occurred in a few patien The cerebrospinal fluid was essentially normal in t patients with central nervous system symptoms. representative cases are described in detail.

61 of the 69 patients were aged less than 9 yea There were 40 males and 29 females. There was higher incidence in Chinese than Thai children th accounted for by the numbers in the general popu tion. The disease was practically absent from Dece ber to May, but incidence increased from June to peak in September–October, after which there was rapid decrease in the number of cases. The incide corresponds with the rainy season.

Autopsies were performed on 5 patients. They show interstitial pneumonitis and scattered haemorrhages the pleurae. Livers were slightly enlarged, pale colour and there was diffuse focal fatty degenerati of liver cells. There were also foci of lymphocyt The spleens were only slightly enlarged and show granulomatous lesions in the Malpighian bodies. The contained monocytoid cells which appeared to fo syncytia. The older, larger lesions resembled tub cles. 3 cases showed enlargement of the mesente lymph nodes; 2 had focal haemorrhages in the hea and patchy myocardial degeneration. The bone marr showed variable numbers of megakaryocytes and pla let-producing megakaryocytes were uniformly fe Virological investigations are in process.

The treatment was intravenous fluids together wi cortisone, which were apparently of dramatic bene Antibiotics were used, but their effect was questionab Of 14 patients who died within 24 hours of admissio 12 died before cortisone therapy could be effective.

C. E. Gordon Smith

BULL. CALCUTTA SCHOOL TROP. MED. 1959, July, v. No. 3, 124–33. **Proceedings of the 11th Sta Conference held on 8th June, 1959. A Ne Disease of Presumptive Viral Aetiology.**

A syndrome characterized by fever, haemorrhag tendency together with necrotic skin lesions over t buttocks developed in all 7 of a group of carpente who were living in one room in a hut in Calcut A neighbouring family was affected and secondary cas occurred in the house of one of the victims who r turned to his village home at the height of his illnes One of the primary cases, 2 village contacts and o of the neighbouring Calcutta family died of th disease.

The initial symptoms comprised fever and vomitin sometimes accompanied by dysenteric bowel motion Gangrenous patches then appeared over the buttock perineum or thighs and later on formed necrotic ulce This might recur later. Bleeding from the gums an haematuria were common. In one fatal case an exte sive haemorrhagic destruction of the wall of the ileu and caecum, with retroperitoneal haemorrhage, w found.

The significant pathological findings comprised leuc penia, thrombocytopenia and anaemia. Leucoagglu nins and platelet agglutinins were demonstrated in t blood. In one patient, who died, grave bone-marro depression was demonstrated.

Attempts to isolate a causal agent were unsuccessful. No constantly present bacterial pathogens were found: eptospirosis was excluded and no actinomycetes were ultured. Material from ulcers and blood serum was noculated into the brains of suckling mice and into mbryonated eggs, but no viral agents were recognized. iltrates obtained from bed-bugs, cockroaches and piders captured in the hut in Calcutta also appeared o be free from viruses, as did larval trombiculid mites f the genus *Schöngastia* removed from rats trapped in the same locality [but the mites were not recovered alive].

The occurrence of anti-leucocyte and anti-platelet bodies in Kyasanur Forest disease, due to an Arbor B virus, was pointed out as suggesting an analogy with that disease, while certain points of resemblance to haemorrhagic fever of Korea were noted. [The latter is presumed to be a mite-borne viral disease.]

J. H. Walters

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

ACT. REVIEWS. 1959, Dec., v. 23, No. 4, 250–72, 1 fig. [92 refs.] **Symposium on Initiation of Bacterial Growth.**

In the *Introduction* (pp. 250–253) S. E. HARTSELL escribes how a physical insult, in this case a freezing emperature, will affect the rate of multiplication after efrosting the cell at 37°C. It was tempting to suppose hat this effect was due to an alteration in generation me, but experimental proof was lacking. Colony election produced substrains with different generation mes but there was no correlation between colony form nd rate of growth. One explanation could be that ome syntheses occur at freezing temperatures but that hose essential for cell division cannot occur until fter defrosting.

The contribution of H. L. CHANCE (*Cytological hanges in early growth phases*, pp. 254–260) has little elevance to the subject of the symposium, but is a seful and condensed description of changes that ccompany (1) spore germination, (2) the growth of ells containing a discrete nucleus or microcyst, and 3) growth in a synchronous culture. Chance aptly emarks that cytologists use methods and techniques which in many cases destroy the system they wish to tudy.

H. C. LICHSTEIN, in discussing *Physiological aspects f growth initiation* (pp. 261–266), points out that rowth and reproduction are separate entities. Growth epends on the suitability of the environment; the ffect of temperature is complex and may increase or lecrease nutritional fastidiousness. *p*H exerts an effect y controlling permeability of the cell to substances ssential for growth; the oxidation-reduction potential nay affect nutritional requirements, but the most important environmental factor is the chemical composition of the medium. For a nutrient to benefit the cell it must be able to get inside and the cell must have the "biochemical machinery" to make use of it.

The *Dormancy, germination, and outgrowth* of bacterial spores are discussed by H. O. HALVORSON (pp. 267–272). Among the substances present in spores and not in the vegetative cell is dipicolonic acid (DPA), which probably exists as a complex in the spore and is responsible for its heat resistance. Spores contain other heat-resistant enzymes which, unlike DPA, can be detected after mechanical rupture of the spore.

The inertness of spores is relative, and the longer a spore suspension is kept, the lower is its viability and the simpler are its germination requirements.

The trigger mechanism for germination is both chemical (L-alanine alone or with other substances such as adenosine) and physical (heat shock at 65°C.). The final stage (outgrowth) follows a burst of metabolic activity which is supported by minerals and nutrients not needed for germination; sulphate is essential at this stage. Thereafter the metabolism is that of the mature vegetative cell.

S. T. Cowan

HUDDLESON, I. F. **Growth of Bacteria in Blood. Use of Cation Exchange Resins for Enhancing or Suppressing Growth.** *Bull. World Health Organization.* Geneva. 1959, v. 21, No. 2, 187–99. [12 refs.]

The author has shown previously [this *Bulletin*, 1958, v. 33, 276] that *Brucella abortus* added to mixtures of cow blood and liquid culture medium multiplied

because the antibacterial system in blood was inactivated by media constituents. Good growth was obtained if an ion exchange resin in the hydrogen phase was added to blood and in the present study this observation has been examined further.

The organisms used were *Brucella abortus, Br. melitensis, Salmonella typhi, Salm. pullorum, Salm. typhi-murium, Shigella flexneri, Pasteurella multocida (septica), Escherichia coli* (bovine mastitis strain), *Staphylococcus aureus* and *Streptococcus agalactiae* (bovine mastitis strain).

The addition of a hydrogen exchange resin to citrated cow blood resulted in an increase in acidity and at *p*H 6·1–6·7 the growth of Gram-negative organisms was enhanced but that of Gram-positive organisms was inhibited—a reversal of the situation obtaining at the normal *p*H of cow blood (*pH* 7·5–7·6). This reversal was not entirely due to the *p*H change because *Salm. typhi, Salm. pullorum* and *Sh. flexneri* did not grow in defibrinated blood at *p*H 6·2 but *Staph. aureus* did.

It was shown that the inhibition of growth of Gram-positive organisms in citrated cows blood acidified with a hydrogen exchange resin was due to the binding of Mg by citrate. When Mg was added to citrated cow blood at *p*H 6·2 *Staph. aureus* multiplied freely. The inhibitory effect of citrated cow blood on the growth of Gram-negative bacteria appeared to be due to 2 components because citrated blood acidified with hydrogen exchange resin did not regain its antibacterial properties unless the *p*H was restored to 7·5 and Mg ions were made available. Neither of these measures alone restored the antibacterial properties of citrat blood.

The addition of both hydrogen and magnesium i exchange resins in appropriate amounts to citrated co blood enabled small inocula of all the organism studied to multiply rapidly and abundantly in blo alone.

Wardlaw *et al.* [this *Bulletin*, 1958, v. 33, 119 showed that Mn or Co can be substituted for M in the properdin-complement system in serum. T effect of these ions on the growth of bacteria in defib nated blood was studied and it was observed that sma amounts of Mn enhanced the growth of *Bruce* species, whereas Co inhibited the growth of *Br. abortu Staph. aureus* and *Strep. agalactiae.*

[The antibacterial action of blood on *Br. abort* was noted even when 5 ml. of blood were dilut with 20 ml. of tryptose broth. As it is common pra tice for 5 ml. of blood (and often more) to be dilut in 10–50 ml. of culture medium for blood culture pu poses there may well be some residual antibacteri effect at this level of dilution. Possibly isolation rat from blood could be improved by the use of these i exchange resins and sodium citrate.] *R. J. Fallon*

Northrop, J. H. **Apparatus for the Maintenance Bacterial Cultures in the Steady State. II. Im proved Turbidity Control and Culture Ce** *J. General Physiol.* 1960, Jan., v. 43, No. 3, 55 4, 2 figs.

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; Other Therapeutic Substances; Disinfection.**

Bliss, Eleanor A. & Alter, B. McD. **Bacterial Resistance to Antibiotics** *in vivo*. **I. Incidence of Resistance.** *J. Bacteriology.* 1959, Nov., v. 78, No. 5, 671–4.

Mice received a large intravenous inoculum of *Staphylococcus aureus*, of which 2 strains were used, and were treated with either penicillin or streptomycin by subcutaneous injection twice daily for 14 days, or were left untreated. Cultures were made from the blood of those dying within 3 days and from the kidney of those dying later (periods of survival are not given). Of 195 cultures from 226 mice treated with streptomycin 4 showed a high degree of resistance to streptomycin and 7 a lower but increased degree. Of 212 cultures from 230 mice not treated with streptomycin (15 had penicillin and the rest nothing) 2 were highly resistant to streptomycin, evidently as a result of spontaneous mutation, but none showed the lower degree of increased resistance. No change in sensitivity to penicillin was seen. [These findings appear to suggest that streptomycin resistance develops less readily *in vivo* than *in vitro*, but their significance might be greater if the duration of treatment before the cultur were obtained was stated.] *L. P. Garrod*

Bauer, A. W., Perry, D. M. & Kirby, W. M. M **Single-Disk Antibiotic-Sensitivity Testing Staphylococci. An Analysis of Technique an Results.** *Arch. Intern. Med.* 1959, Aug., v. 10 No. 2, 208–16, 8 figs. [16 refs.]

This paper is a plea for a single disc of fairly hi antibiotic content (varying from 10 units of penicill to 100 μgm. of streptomycin) for testing bacter sensitivity, based on tests with 2,000 strains of staphyl cocci. [Separate results are given for coagula positive and -negative strains: they differ little, a the authors do not explain why they devote so mu attention to a normally non-pathogenic organism The frequencies of different diameters of inhibiti zones are plotted as graphs, and those for chlora phenicol, tetracycline and erythromycin show 2 wid separated peaks with very few strains in the int mediate zone: *i.e.*, most strains were either ful

ensitive or clearly resistant to these antibiotics. The listribution of penicillin resistance is similar, although iot quite so clear cut: that to streptomycin is more ariable: the curves for neomycin and bacitracin have nly a single peak because almost all strains were ensitive. A table gives zone diameters for each antiiotic which should be interpreted as meaning sensitive, ntermediate or resistant. Parallel tests with chloramhenicol of 108 strains by a tube dilution method howed good correlation with the disc method in all but instances. *L. P. Garrod*

VÁCZI, L., JENEY, E. & GÉDER, L. **The Relation of Surface Properties and Antibiotic Resistance in** *Staphylococcus aureus.* **I. Phage-Typing of Polyresistant** *Staphylococcus aureus* **Strains.** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 3, 249–55. [13 refs.]

Staphylococcus aureus strains were isolated from dult patients and from patients and staff in the infants' lepartment of a hospital in Hungary [the majority of trains were "from skin or throat conditions, some from ther infections"]. They were phage typed and tested gainst the 6 common antibiotics. Of the 355 strains ·6% were sensitive to all antibiotics, 51% were resisant to 1; 14·1% to 2; 6·7% to 3 or 4 and 18·4% o 5 or 6 antibiotics.

The number of non-typable strains was high (30·4%) nd non-typable strains accounted for 11·8% of fully ensitive strains, 50% of strains resistant to 3 or 4 ntibiotics and 88% of strains resistant to 5 or 6 antiiotics. 6 of the 8 typable polyresistant strains belonged o Group III.

Of the 115 strains isolated from the infants' departnent 42 (36·5%) were polyresistant and 39 of these vere non-typable. 64 were resistant to 1 or 2 antiiotics and less than 10% of these were non-typable.

The authors suggest that the predominance of nonypable strains may be explained by the difference in acterial surface of the sensitive and polyresistant trains. [It is not clear how far the polyresistant nonypable strains examined here may be examples of a ingle "epidemic" type present in the hospital at the ime of the investigation.] *M. Patricia Jevons*

BARBER, Mary, DUTTON, A. A. C., BEARD, M. A., ELMES, P. C. & WILLIAMS, R. **Reversal of Antibiotic Resistance in Hospital Staphylococcal Infection.** *Brit. Med. J.* 1960, Jan. 2, 11–17, 4 figs. [16 refs.]

This important paper gives the results of a large-scale linical experiment connected with the use of antiiotics which has been in progress at Hammersmith Hospital, London (Postgraduate Medical School of Medicine). Its inception was preceded by adopting a ariety of "anti-cross infection measures", including solation of infected patients and improved methods of terilization and disinfection, which may have contriuted to the results obtained. The experiment, as it oncerned antibiotics, consisted of adopting a policy or their use throughout the hospital the main features f which were general restriction of their prophylactic use, abandonment of the use of penicillin except in a few specified wards, and "the general employment of double chemotherapy, each drug being given in full dosage". Recommended combinations for various common purposes are listed. The effect of this on antibiotic consumption was to divide that of penicillin by 2·6, and to multiply that of tetracycline, chloramphenicol, erythromycin and novobiocin by 1·8, 2·0, 2·5 and 6 respectively.

From 6 months before this policy was adopted to 15 months after its introduction records have been kept of the frequency of staphylococcal infection and of the frequency of resistance to different antibiotics in the staphylococci causing it. The frequency of staphylococcal infections of all kinds fell from 10% to 7% of patients and that of serious infections (including 49 generalized infections with 24 deaths) diminished considerably more than this: these serious infections were almost all due to strains with multiple antibiotic resistance. The frequency of resistance to both penicillin and tetracycline in strains isolated from patients diminished substantially; that of resistance to erythromycin rose initially but has fallen again. Penicillin resistance also became less common in strains from nasal carriers among nurses. It thus appears that by the general adoption in a hospital of such a policy for the use of antibiotics, the trend towards increasing resistance to antibiotics in staphylococci can be checked and indeed reversed. For details of the changes observed and for a discussion of their significance which is commendably cautious and far from suggesting that this problem has been solved, the original paper should be consulted. *L. P. Garrod*

EPP, Marguerite. **Serological Procedure for the Detection of Antibodies to Penicillin.** *Science.* 1959, Nov. 27, v. 130, 1472.

Penicillin T (*p*-aminobenzyl penicillin) or penicillin V [the author does not say why he used these in preference to penicillin G] can be coupled to human Group O cells by means of bis-diazotized benzidine. Such cells were agglutinated to titres varying from 4 to 64 by the sera of 9 out of 20 persons "with reported allergic manifestations to penicillin". The addition of small amounts of penicillin inhibited this reaction. Details for preparing the cells and conducting the test are given. *L. P. Garrod*

BALLIO, A., CHAIN, E. B., DI ACCADIA, F. D., MASTROPIETRO-CANCELLIERI, Maria F., MORPURGO, G., SERLUPI-CRESCENZI, G. & SERMONTI, G. **Incorporation of α,ω-Dicarboxylic Acids as Side-Chains into the Penicillin Molecule.** [Correspondence.] *Nature.* 1960, Jan. 9, v. 185, 97–9.

This paper from the International Centre for Chemical Microbiology, Rome, reports that by adding adipic or other related acids to the fermentation medium, a penicillin was obtained with much greater activity against Gram-negative and lesser activity against Gram-positive organisms than benzyl-penicillin. This proved to be (4-carboxy-*n*-butyl)-penicillin, which

is related in structure and very similar in antibacterial spectrum to the form of penicillin known as cephalosporin N [this *Bulletin*, 1953, v. 28, 976]. It is mentioned that 7 subjects highly allergic to benzyl penicillin did not react to this substance. [Cephalosporin N, or synnematin B, has been commended for the treatment of typhoid fever, but is unobtainable, supposedly because of difficulties in production. If the penicillin described in this paper proved to have other necessary properties not dealt with here, and could be more easily produced than cephalosporin N, it might have a therapeutic future.] *L. P. Garrod*

ANAND, N.; DAVIS, B. D.; ARMITAGE, A. K. **Effect of Streptomycin on** *Escherichia coli*. [a] **Damage by Streptomycin to the Cell Membrane of** *Escherichia coli* [ANAND & DAVIS]. *Nature*. 1960, Jan. 2, v. 185, 22–3. [b] **Uptake of Streptomycin by** *Escherichia coli* [ANAND, DAVIS & ARMITAGE]. *Ibid.*, 23–4, 1 fig.

These papers are from the Department of Bacteriology and Immunology, Harvard Medical School. In the first it is reported that when 60 μgm./ml. streptomycin is added to multiplying cultures of *Escherichia coli* in a mineral-glucose medium, nucleotides are liberated in differing, but—for some of the 7 estimated, large—amounts, greater than those initially present in the cells. There was also a 4-fold increase in the "excretion" of amino acids, a loss of capacity to concentrate valine, and an increased permeability to citrate. Streptomycin must therefore act on a permeability barrier, which is believed to be the cell membrane. Chloramphenicol, 20 μgm./ml. prevented both bactericidal action and nucleotide excretion.

The second paper describes studies of the absorption of streptomycin by *E. coli*, carried out with streptomycin labelled with ^{14}C. There was an initial very rapid uptake, complete within 1 minute, after which the cell content remained stationary for 15 minutes (according to the text: 10 minutes in a chart). This is about the time when nucleotide excretion had been shown to begin. Uptake continued until after 1 hour the cell content had risen further about 3-fold. This secondary uptake is attributed to the increased permeability produced by damage to the cell membrane in the first stage. The presence of chloramphenicol prevented secondary uptake, and the addition of toluene or polymyxin, which damage the cell membrane, increased it. The authors are uncertain whether damage to the cell membrane in the first stage is "a sufficient as well as a necessary cause of the bactericidal effect", or whether this has to be completed by penetration, although they found that a resistant mutant had the same initial, but no secondary, uptake. This mechanism is believed to explain synergy between streptomycin and other bactericidal agents, the damage of one permitting penetration by the other. *L. P. Garrod*

DILL, W. A., THOMPSON, E. M., FISKEN, R. A. & GLAZKO, A. J. **A New Metabolite of Chloramphenicol.** [Correspondence.] *Nature*. 1960, Feb. 20, v. 185, 535–6.

GITTINGER, W. C. & WIENER, H. **The Activation b Glucosamine of the Absorption of Tetracyclin into the Systemic Circulation.** *Antibiotic Me* New York. 1960, Jan., v. 7, No. 1, 22–7, 1 fig.

"A statistically balanced, double-blind, triple cros over study was conducted in 122 healthy men compare glucosamine, citric acid, and phosphate cor plex for ability to increase absorption of tetracycli from the gastrointestinal tract. They were also cor pared for their ability to raise serum levels of t antibiotic beyond those produced by equal amounts uncombined tetracycline. Serum levels were measur 2, 3, and 6 hours after ingestion of 250 mg. of t tetracycline preparations.

"At all hours, tetracycline potentiated by glucosami produced serum levels almost double those of u potentiated tetracycline. At all hours, the glucosami preparation produced antibiotic serum levels higher th either the citric acid preparation or the preparati of tetracycline phosphate complex. The glucosami preparation gave the most consistent elevation of seru levels of all tetracycline preparations tested.

"No correlations were found between serum leve and age or weight of the subjects when tetracycli hydrochloride was administered orally."

ROKOS, J., MÁLEK, P., BURGER, M., PROCHÁZKA, P. KOLC, J. **The Effect of Divalent Metals on t Inhibition of Pancreatic Lipase by Chlortetr cycline.** *Antibiotics & Chemotherapy*. New Yor 1959, Oct., v. 9, No. 10, 600–608, 6 figs. [39 refs.

These authors from Prague argue that since tetr cyclines may act by interfering with bacterial enzyr systems, a study of the conditions under which th interfere with other enzymes may be helpful. secondary consideration is that some such effect as th demonstrated here may actually be produced in t bowel. The enzyme action studied was that of lipa on glyceryl tributyrate. Chlortetracycline was fou to inhibit this only in the presence of divalent meta the order of activity of which was $Co^{++} > Zn^{++} > Mn^{++} > Ca^{++} > Mg^{++} > Ba^{++}$. Much low concentrations of chlortetracycline were inhibitory *p*H 7·9 than at 6·1. The inhibitory effect was abolish by the addition of sodium citrate. *L. P. Garrod*

HALL, R. H. & GALE, G. O. **Augmentation of Chlo tetracycline Activity against Two Strains** *Staphylococcus* **by Kinetin.** *Proc. Soc. Exp Biol. & Med.* 1960, Jan., v. 103, No. 1, 234 3 figs. [14 refs.]

"1. Kinetin, although non-toxic to an antibiot resistant strain of *Staphylococcus albus*, augmented t action of chlortetracycline against this microorganis *in vitro*. 2. Some other 6-(substituted amino) purin had this property. 3. Kinetin caused a slight but stat tically significant increase in activity of chlortetracycli and tetracycline against an antibiotic-sensitive strain *Staphylococcus aureus* in mice."

REYNOLDS, H., HILDEBRAND, J. F., LIVINGOOD, C. S. & FOSNAUGH, R. P. **Clinical Features of Contact Dermatitis due to Neomycin. Report of Cases.** *Arch. Dermat.* 1959, Oct., v. 80, No. 4, 455–60.

These authors have seen 28 patients in whom the local application of neomycin for treatment of various forms of dermatitis has apparently resulted in sensitization to the antibiotic. The histories of 6 are given in detail. They emphasize that the development of the condition is insidious, and usually mistaken at first for a simple exacerbation of the condition being treated. Intradermal or patch tests for sensitivity or both were positive in most of the patients so tested. The area of a patch test commonly became and remained eczematous for 5–7 weeks: in 1 patient this condition persisted for 7 months. *L. P. Garrod*

COFFEY, G. L., ANDERSON, Lucia E., FISHER, M. W., GALBRAITH, Margaret M., HILLEGAS, A. B., KOHBERGER, Dorothy L., THOMPSON, P. E., WESTON, Kathleen S. & EHRLICH, J. **Biological Studies of Paromomycin.** *Antibiotics & Chemotherapy.* New York. 1959, Dec., v. 9, No. 12, 730–38. [10 refs.]

"Paromomycin is a broad-spectrum, water-soluble, basic antibiotic obtained from culture filtrates of a strain of *Streptomyces* that closely resembles *Streptomyces rimosus* NRRL 2234. Fermentation and assay methods are presented. Subcutaneous administration of this antibiotic proved effective in experimental bacterial infections with strains of *Escherichia, Klebsiella, Paracolobactrum, Proteus, Shigella,* and *Staphylococcus,* and oral administration was effective in protozoal infections with *Entamoeba* and *Trichomonas.* Paromomycin was well tolerated by laboratory animals. Toxicity was observed only following the parenteral administration of high dosages, and this was limited to the kidneys. Mild renal damage, which was reversible after withdrawal of the drug, was observed when moderate dosage levels were administered parenterally for prolonged periods. Paromomycin is apparently poorly absorbed from the intestine, as shown by low and transient blood titers and high fecal values. Although only a small part of the oral dose is recoverable in the urine, high drug-urine levels are obtained. The fortunate combination of high antiamebic and antibacterial activity and low oral toxicity makes paromomycin unique among the available drugs and suggests that it should be a useful therapeutic substance."

HASSALL, C. H. & MAGNUS, K. E. **Monamycin: a New Antibiotic.** [Correspondence.] *Nature.* 1959, Oct. 17, v. 184, Suppl. No. 16, 1223–4.

This paper is from the Chemistry Departments of the University College of Swansea and of the University College of the West Indies, Jamaica. Monamycin is formed by an organism now named *Streptomyces jamaicensis*: this was originally isolated during a soil survey aimed at discovering organisms antagonistic to the *Fusarium* causing Panama disease of the banana plant. The extraction and some physical and chemical properties of this antibiotic are briefly described. It is highly active against Gram-positive organisms, including staphylococci resistant to other antibiotics, and inactive against the only 2 Gram-negative species mentioned as having been examined. Mice survived subcutaneous injections of 850 mgm./kgm. [The solubility in water is not stated. If the expression "<1/100,000" in the table of anti-bacterial activities is any indication of this, the material injected into mice must have been a suspension which may have been absorbed very slowly, and this experiment should be interpreted accordingly.] *L. P. Garrod*

MACWILLIAM, I. C. **A Survey of the Antibiotic Powers of Yeasts.** *J. General Microbiol.* 1959, Oct., v. 21, No. 2, 410–14. [15 refs.]

This paper from the Brewing Industry Research Foundation reports that 153 strains of yeasts of many different genera have been examined for antibiotic formation. No action was detected on any of 6 species of bacteria, and the only instance of an action on fungi was inhibition by *Candida pulcherrima* of the growth of some species of *Fusarium, Penicillium* and *Mucor*: this effect is attributed to the formation of pulcherriminic acid. The author concludes that "yeasts are not a promising source of antibiotics". *L. P. Garrod*

ZSOLNAI, T. Versuche zur Entdeckung neuer Tuberkulostatika. VII. Die mit verschiedenen Aldehyden und Ketonen gebildeten Derivate des Salicylsäurehydrazids und des 5-Brom-salicylsäure-hydrazids. [**Experiments for the Discovery of New Tuberculostatic Drugs. VII. Different Aldehyde and Ketone Compounds of Salicylic-Acid-Hydrazide and of 5-Bromium-Salicylic-Acid-Hydrazide**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 7/8, 539–52. [15 refs.] VIII. Phenolische Hydroxyl-Radikale enthaltende Imidazolin- und Benzimidazol-Derivate. [**VIII. Imidazoline and Benzimidazole Compounds containing Phenolic Hydroxyl Groups**] *Ibid.*, 553–7.

These 2 papers will be of interest chiefly to chemists. The author has synthesized many new compounds related to existing drugs used in the treatment of tuberculosis, and defines their structure and properties at considerable length. Having determined their minimum inhibitory concentration for *Mycobacterium tuberculosis* H37Rv in Kirchner's medium with 10% serum, he discusses such relationships as there appear to be between their structure and their activity as demonstrated in this test. The general nature of the 2 series of compounds is conveyed in the titles of the papers. The first deals with a series of 24 compounds, the 2 most promising of which were also submitted to a therapeutic test in guineapigs which showed them to have no *in vivo* activity. The second paper deals with 6 compounds only which possessed moderate *in vitro* activity but were not tested *in vivo*. *L. P. Garrod*

HESS, H. & SPEISER, P. **Comparative Efficacy of Bactericidal Compounds in Buffer Solutions. Part I.** *J. Pharmacy & Pharmacol.* London. 1959, Nov., v. 11, No. 11, 650–58, 4 figs. [28 refs.] Part II. *Ibid.*, 694–702, 6 figs. [25 refs.]

I. These experiments were performed with numerous phenols and aromatic alcohols, 2 organic mercury compounds, 2 quaternary ammonium compounds, and with multiple strains of 3 Gram-negative and 3 Gram-positive organisms. The first paper describes the method used, which consisted of mixing germicide solution and bacterial suspension, both in phosphate buffer at *p*H 7·0, maintaining at 20° or 37°C. for 30 minutes or longer, passing the whole of the test mixture through a membrane filter followed by a large volume of water, and cultivating the filter on a nutrient agar plate, on which the colonies were subsequently counted. Examples are given of variations between the results of replicate tests, some of which are wide. The method is nevertheless commended for any test of a germicide which demands a certain percentage kill as distinct from sterilization. Observations were also made on the relative merits of different culture media, and on the viability of the test organisms in the buffer solution.

II. The second paper gives a selection of the results obtained (these papers are condensed from a thesis by Hess for the degree of Ph.D. in the University of Basle). The factor most emphasized in the experiments of which detailed results are given (in the form of diagrams showing numbers of survivors) was *p*H: all tests were done at *p*H 4, 5·5, 7 and 8·5. Phenols were found to be least active at about *p*H 5·5 against Gram-negative organisms, although Gram-positive species obeyed the usually accepted rule of the greater activity of phenols in acid media. In connexion with phenols generally a hypothesis is proposed that activity varies with solubility in the lipids of the bacterial cell surface. A new compound, 4-chloro-β-phenylethyl alcohol, is considered to have promising properties. Of mercury compounds, phenyl mercuric borate was more active in alkaline solution, thiomersal in acid. The 2 quaternaries domiphen bromide and cetyl pyridinium chloride both performed better in alkaline solutions, although the activity of the latter was less affected by *p*H. Results with these compounds were erratic, and some inquiry was made into the reason for this.

L. P. Garrod

COOK, A. M. & STEEL, K. J. **The Antagonism of the Antibacterial Action of Mercury Compounds. Part III. The Effects of certain Sulphydryl Compounds on *E. coli* I.** *J. Pharmacy & Pharmacol.* London. 1959, Dec., v. 11, Suppl., 157 T-161 T. [16 refs.] **Part IV. Qualitative Aspects of the Antagonism of the Antibacterial Action of Mercuric Chloride.** *Ibid.*, 162 T-168 T. [14 refs.]

The first paper describes experiments to determine whether substances used to antagonize the action of mercury compounds can themselves interfere with bacterial growth, the only organism used being *Escherichia coli*. They were included either in the diluent use in preparing the inoculum, or in the solid mediu surface-inoculated from this, the result being judge by comparing colony counts with those given by norm diluent and medium. Some reductions in these coun were seen, and the authors conclude that the followin concentrations (gm.%) should not be exceeded: cystei 0·25, glutathione 0·25, thioglycollate 0·1, dimercapro 0·05. Horse serum had no inhibitory effect in an concentration up to 20%.

The second paper is a quantitative study of th neutralizing action of these substances on that of me cury perchloride on *E. coli*. By varying the amoun of both in peptone water then inoculated and observe for growth, it was shown that about 2 molecules eac of cysteine, glutathione and thioglycollic acid and 1 c dimercaprol were necessary to antagonize 1 molecu of mercury perchloride. When the latter was adde first and the antagonist 30 minutes later, the necessar molecular ratio permitting growth increased (*e.g.* cysteine 3·2:1, dimercaprol 1·4:1): larger ratios sti were required after exposure of bacteia to the germicid in water instead of peptone water, or after more pr longed exposure. Serum, although apparently exertin some neutralizing effect when present from the star had no "reviving" effect. *L. P. Garrod*

MINTO, W. L. & NEWMAN, B. **Antiseptic Activity o Beta-Amylose Triiodide.** *Antibiotics & Chemo therapy.* New York. 1959, Sept., v. 9, No. 530–34.

A heavy inoculum of broth cultures of 8 species c Gram-positive and 5 of Gram-negative bacteria wa added to falling dilutions of beta-amylose triiodide i distilled water, and cultures were made from thes after ½, 1, 2 and 5 minutes. The tables of resul show that a concentration of 0·08% killed almost a species in 2 minutes or less (5-minute results are no given). Serum and other forms of organic matter ha little or no interfering effect. Mice given an intra peritoneal inoculum of pneumococcus culture which wa uniformly lethal in controls regularly recovered whe given a single injection of beta-amylose triiodide solu tion by the same route, the dose being 120 mgm./kgm 15 minutes after inoculation, or smaller repeated dos (the smallest used being 50 mgm./kgm.) starting 1, or 2½ hours after inoculation. *L. P. Garrod*

EISENBERG, G. M., WEISS, W., SPIVACK, A. P. FLIPPIN, H. F. **Preliminary Studies of the Ant bacterial Activity of a Plastic Spray containin Tetramethylthiuramdisulfide intended for Us on the Skin.** *Antibiotic Med.* New York. 195 Oct., v. 6, No. 10, 594–600, 1 fig. [12 refs.]

The preparation with which this paper is concern is a solution of a methacrylate resin in ethyl aceta also containing tetramethylthiuramdisulphide (TMTI together with "propellants": when sprayed on the ski this leaves a film of the resin containing the antisepti

TMTD, and this application is proposed as a substitute for post-operative wound dressings.

These authors began by adding TMTD dissolved in acetone to nutrient agar to give a final concentration of 0·25%, and inoculating this with multiple strains (165 in all) of staphylococci, *Streptococcus faecalis*, and various coliform bacilli: the growth of all of these was inhibited for 1 day, and of 142 for 2 days. Secondly it was shown that TMTD diffuses out of the plastic film by spraying it on to filter paper discs and placing these on plates inoculated with staphylococci: zones of inhibition were produced surrounding these, and were re-produced with little diminution in size when the disc was transferred from plate to plate through 4 cultures. Thirdly they sprayed the film on the skin of patients, removed it after 3 hours, applied a "multiple contact point sampler" to the area, and with this inoculated a blood agar plate. Compared with a sample so obtained before application of the film, this showed an average reduction in colonies per sq. inch of skin from 118·3 to 1·8. In case this might have been due to the physical removal of bacteria by adherence to the film, the same experiment was done with the same material and with a "polyvinyl alcohol type plastic spray", neither containing TMTD, and a similar result was obtained [no details given], but the authors are not disconcerted by this; they add that subcultures of films lacking TMTD showed evidence of bacterial growth, while those of films containing it did not. They are now conducting a controlled study to determine whether the use of this spray will reduce the incidence of post-operative wound infection. *L. P. Garrod*

Van Der Schaaf, A., Jaartsveld, F. H. J. & Van Maanen, P. H. A. M. Proeven over ontsmetting van de huid. II. [**Experiments on Disinfection of the Skin. II**] *Tijdschr. v. Diergeneesk.* 1960, Feb. 15, v. 85, No. 4, 187–96.

The English summary appended to the paper is as follows:—

"Hibitane (chlorhexidine), Cetavlon (cetyltrimethyl ammoniumbromide) in a concentration of 1% and different chloramines in a concentration of 0.4% appeared to be the only antiseptics of a number of tested disinfectants mentioned in table 1 which could kill totally within 3 minutes *Staphylococcus aureus*, *Salmonella dublin* and *Brucella abortus* (Str. 19) on and in the superficial layers of the skin without irritating the epidermis.

"Bacterial spores could not be killed even in the highest concentrations by suitable disinfectants within a short time.

"The proteins of milk partly inhibit the disinfecting capacity of chloramine and to a lesser degree that of Hibitane.

"Hibitane diacetate is precipitated and inactivated by sodium chloride in physiological concentrations and by urine.

"The Rideal-Walker test is less suitable for testing antiseptics for the human or animal skin than the "teat-test" which is simple and gives reproducible results even with disinfecting pastes and barrier creams."

Ministry of Health. Central Health Services Council. **Hospital Laundry Arrangements. Report of the Committee** [Cunliffe, Chairman]. 22 pp. 1959. London: H.M. Stationery Office. [1s. 3d.]

The scope of this report is adequately described in its official terms of reference:—

"To investigate and report on hospital laundry arrangements with particular regard to the avoidance of infection in the handling of fouled and infected linen, and the maintenance of adequate control over stocks of linen and other articles under such arrangements."

Over a period of 3 years evidence was collected from various interested bodies and a number of visits were made to hospitals and laundries.

The report is presented in 2 sections. The first is concerned with the avoidance of infection, and attention to various ways in which this can be achieved. Particular emphasis is laid on centralization: it is recommended that foul linen should be transported in closed containers to central sluicing points, with a minimum of handling at ward level. Machinery should be developed to allow as much as possible of the processing to be done automatically. Special attention should be paid to the movement of staff between the sorting room and other relatively clean areas, to the health of such staff, and to the separation of staff working in the clean and dirty side of the laundry. The need for more research into techniques for disinfecting and washing is stressed, as is that for standardizing codes of practice and disseminating reliable information widely and quickly to all who are concerned with these problems.

The second section deals with the control of stocks of linen and is largely administrative in character.

One point that emerges from both sections is that time spent in counting linen is largely wasted. The report recommends that soiled linen should not be counted at all (an important measure in the avoidance of infection) and that the counting of clean linen should be reduced to a minimum. This can be done by instituting a central linen room, from which daily issues are made to the wards, where only small stocks are held.

Although this report is concerned mainly with principles, and leaves their detailed application to individual hospitals, it is most valuable and should be studied not only by administrative committees but also by those charged with the control of infection in hospitals. *J. C. Kelsey*

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

NETER, E. & GORZYNSKI, E. A. **Studies on Indirect Staphylococcal Hemagglutination.** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Oct.–Nov., v. 118, Nos. 4/5, 269–88. [22 refs.]

Human erythrocytes were sensitized with the supernatant fluid from cultures of a number of strains of staphylococci [which are not characterized further] and tested for agglutination by pooled human gamma-globulin. [There is no indication of the nature of the antigen-antibody system being explored in this way.] The sensitivity of the test was increased by treatment of the red cells with various proteolytic enzymes. Different staphylococci had differing sensitizing effects. The haemagglutinating factor could be absorbed from the gamma-globulin solution by some strains of *Bacillus subtilis*. *R. E. O. Williams*

PARKER, M. T. & SIMMONS, L. E. **The Inhibition of *Corynebacterium diphtheriae* and other Gram Positive Organisms by *Staphylococcus aureus*.** *J. General Microbiol.* 1959, Oct., v. 21, No. 2, 457–76, 2 text figs. & 4 figs. on pl. [23 refs.]

Strains of *Staph. aureus* were bacteriophage-typed and tested for their ability to inhibit the growth of *Corynebacterium diphtheriae mitis* No. 51. The inhibition test was considered positive (DI +) when the zone was 1 mm. or more in radius. Over 93% of type 71 strains which are usually associated with superficial skin lesions produced sharp zones of inhibition (DI + S). Inhibition of this kind was shown by only a few other strains most of which were also of Group II or were not typable, they had also been isolated from skin lesions and had other properties characteristic of type 71 strains. 2·6% of all strains produced hazy zones of inhibition (DI + H): the majority were not typable or unclassifiable but there were representatives of all phage groups except Group II.

The agents producing both types of inhibition were diffusible through agar but not through cellophan. Cell-free preparations could not be obtained.

Variable results were obtained when 40 other corynebacteria were tested for inhibition by staphylococci of various types. On the whole DI + S strains of types other than type 71 were less active against other corynebacteria than type 71 strains. Some DI + S strains inhibited all DI − and DI + H strains tested but this inhibition was weak.

DI + S strains lost their inhibitory activity in one step after a few months storage. This was accompanied in most cases by the acquisition of susceptibility to phage 55 but not by changes in other cultural characteristics. DI + H strains were not affected by storage.

No carried phage could be detected in the DI + S strains the loss of which might account for the gain in susceptibility to phage 55. DI-variants lysogenized with phage 55 remained DI −. *M. Patricia Jevons*

NORTH, E. A. **The Use of Specific Antitoxin against Experimental Staphylococcal Infection in Mice.** *Australian J. Exper. Biol. & Med. Sci.* 1959, Aug. v. 37, Pt. 4, 341–52. [22 refs.]

The effect of antitoxin in protecting mice against intra-peritoneal challenge with staphylococci was examined. 4 suspending materials were used for the challenge doses: BOAKE's clotting mixture (1% fibrinogen and 1% plasma) [this *Bulletin*, 1956, v. 31, 949] with 150 × 10^6 cocci, 5% mucin with 12 × 10^6 cocci, saline with 4,000 × 10^6 cocci and broth with 500–750 × 10^6 cocci. When antitoxin was given 24 hours before challenge with the clotting mixture or mucin suspensions there was significant protection; when the interval was 4 hours there was no protection. This effect was less marked with the saline and not seen broth suspensions. Active immunization had some protective effect, which was reduced by administration of antitoxin 2 hours before challenge. In a few experiments diphtheria antitoxin, given 24 hours before challenge with the staphylococci, had some protective effect.

R. E. O. Williams

RICHOU, R. & RICHOU, H. Antibiotiques et agglutinines antistaphylococciques. **[Antibiotics and Anti-staphylococcal Agglutinins]** *C.R. Soc. Biol.* 195- v. 153, No. 6, 969–71.

Neither penicillin nor streptomycin, administered repeatedly to rabbits undergoing a course of inoculation with a killed staphylococcus vaccine, had any detectable effect on the production of agglutinins.

R. E. O. Williams

HOLLINGER, Nell F. & RANTZ, L. **In Pursuit of the *Streptococcus*. Newer Techniques for their Recovery and Identification, and Clinical Implications.** *Pediatrics.* Springfield Ill. 1959, Dec., 24, No. 6, 1112–17, 2 figs. [15 refs.]

2 Dacron-tipped swabs were used to sample the throat; 1 was transported to the laboratory in desiccant the other was used to inoculate first a filter paper strip [this *Bulletin*, 1959, v. 34, 167] and then a control blood agar plate. The filter paper slip was plated after 2–3 days and examined for haemolytic streptococci. The comparison of filter paper strip with direct plating comprised 1,017 patients, 186 of whom yielded haemolytic streptococci—88 by both methods, 18 by the control only, and 80 by filter paper strip only. In 552 patients the yield from the Dacron swab held in desiccant was compared with the direct plating; 32 yielded streptococcus by both methods, 12 only by the control and 16 only by the Dacron-desiccant swab.

R. E. O. Williams

LEEDOM, J. M. & BARKULIS, S. S. **Studies on Virulence of Group A β-Hemolytic Streptococci.** *J. Bacteriology.* 1959, Nov., v. 78, No. 5, 687–94. [21 refs.]

Properties of mouse virulent variants of a Group A *Streptococcus pyogenes* type 14 (strain Q496) were compared with those of the parent avirulent culture.

Serial mouse passage of the avirulent Q496 (LD50, 500,000 chains) was performed to facilitate the isolation of variants of enhanced virulence. The organisms isolated after 22 passages was designated Q22× (LD50, 100 chains) and after 43 passages, Q43× (LD50, 25 chains). Viable cocci of Q496 rapidly disappeared when injected intraperitoneally into mice in contrast to a rapid multiplication of cultures of Q22× and Q43×. The Q496 strain was phagocytosed by human neutrophils but cocci of strains Q22× and Q43× were not ingested. Surprisingly, in the indirect bacteriostatic test [this *Bulletin*, 1945, v. 20, 768] human leucocytes did not inhibit the multiplication of any of the 3 strains. Addition of type 14 rabbit antiserum to the system enabled the leucocytes to inhibit completely multiplication of the Q22× and Q43× strains. M precipitin antigen was not present in cell wall extracts of Q496 but was present in similar extracts of Q22× and Q43×. Q43× had a significantly lower glycolytic rate compared to the other 2 strains. Noticeably less streptolysin S was produced by the virulent strains.

[The relationship of mouse virulence and antigenic structure in haemolytic streptococci has been known for many years. (LANCEFIELD, *Harvey Lectures* 1940, ser. 36, 251). The surprising finding that the glossy variant containing no demonstrable M antigen could survive in heparinized whole human blood is possibly related to the recent demonstration that certain type 14 strains carry 2 distinct M antigens. No data are given indicating that the type 14 antiserum used contained antibody directed against both M antigens.]

H. Gooder

GRAM, H. G. & BÖHMIG, R. Experimentelle Untersuchungen mit Fraktionen der Leibessubstanzen der A-Streptokokken. [**Pathogenic Properties of Fractions of Group A Streptococci**] *Ztschr. f. Immunitätf. u. Exper. Therap.* 1960, Jan., v. 119, No. 1, 1–94, 16 figs. [Numerous refs.]

The English summary appended to the paper is as follows:—

"The pathogenic action in animals of group specific polysaccharides of group A streptococci and a fraction named streptococcal protein were investigated. The following results were reported:

"1. Group specific substance C administered intravenously has no affinity to a special sort of tissue.

"2. Greater amounts of substance C induce anaphylaxis.

"3. Though being a hapten, substance C induces changes principally similar to those characteristic for antigen-antibody reactions.

"4. Very small amounts of streptococcal protein produce a considerable leucocytosis.

"5. No special localization of these changes could be observed.

"6. The course of tissue reactions in rabbits immunized actively with streptococci are described.

"7. The tissue reactions in rabbits immunized actively correspond to the changes produced by antigen-antibody reactions, i.e. arteriitis, proliferation of small vessels, myocarditis, myocardial necrosis.

"8. These tissue reactions are not altered, neither quantitatively nor qualitatively by non-fatal anaphylactic shock.

"9. A single antigen-antibody reaction induces long lasting histological changes.

"10. The attempts to produce rheumatic granulomas failed, only histocytical proliferations developed.

"The possibilities to explain tissue changes following immunological phenomena are discussed, especially the rôle of proteases and of complement.

"There is no doubt that antigen-antibody reactions play a rôle in the pathogenesis of rheumatic fever. Unknown additional factors are needed for the production of characteristic tissue reactions."

GINSBURG, I. & GROSSOWICZ, N. **A Cell-Bound Hemolysin of Group A Streptococci.** *Bull. Res. Counc. of Israel.* 1958, Dec., v. 7E, No. 4, 237–46. [11 refs.]

During the growth of streptococci in a synthetic medium [this *Bulletin*, 1958, v. 33, 275] it was observed that the haemolytic potency of the whole streptococcal culture was always much higher than that of supernatants obtained from such cultures. This paper records observations on the nature and production of this cell-bound haemolysin.

The haemolysin was demonstrated by the addition of rabbit or human red blood cells to a washed suspension in buffered saline of *Streptococcus pyogenes* strain S84 Type 3 (previously incubated for 5 minutes at 37°C.). The presence of a fermentable sugar, Mg++ and cysteine in the suspending medium increased the haemolytic activity 75-fold. Cell-bound haemolysin was released from the bacterial cells into solution by surface active materials, *e.g.*, Tween 40 and 80, Triton and by crystalline albumin. Released haemolysin has been designated streptolysin D (SLD, D for detergent). Differentiation of SLD from previously described streptococcal haemolysins, streptolysin O (SLO) [this *Bulletin*, 1939, v. 14, 423], streptolysin S (SLS) [*ibid.*, 1949, v. 24, 88] and intracellular haemolysin (IH) [*ibid.*, 1956, v. 31, 864] was as follows. Unlike SLO, SLD is not inhibited by cholesterol or anti-streptolysin O. Sonic oscillation of the washed streptococcal culture [which is reported to release IH, *ibid.*, 1956, v. 31, 864] did not liberate SLD. The SLD forming system (glucose $MgSO_4$ tween) differs from the SLS forming system by (1) not requiring ribonucleic acid and maltose for lysin formation, (2) a more rapid rate of haemolysin production by resting cells, and (3) a greater resistance to UV irradiation and the action of M/100 phenylserine.

The authors do not rule out the possibility that SLS and SLD are a single haemolysin produced by separate metabolic processes differing in sensitivity to the agents described. Both SLS and SLD are apparently non-antigenic.

H. Gooder

KANTOR, F. S. & COLE, R. M. **A Fibrinogen Precipitating Factor (FPF) of Group A Streptococci.** *Proc. Soc. Exper. Biol. & Med.* 1959, Oct., v. 102, No. 1, 146–50, 1 fig. [10 refs.]

Partially purified M protein of Type I haemolytic streptococci was found to produce rapid precipitation of various mammalian plasmas and fibrinogen. This precipitating factor (FPF) was subsequently found in acid extracts of at least 1 of every type of Group A streptococcus when 2 or more strains were available for testing; reactivity, however, did not correlate with the ability of the strain to react with type specific serum. Strains of type 18 reacted with fibrinogen only after the M extract was concentrated by alcohol precipitation. FPF was found in extracts of 1 group G strain but not in extracts of 14 streptococci other than Group A, nor was it found in extracts of coagulase positive staphylococci, pneumococci, or α-haemolytic streptococci tested. T extracts of strains producing FPF did not precipitate fibrinogen.

Removal of M protein by pepsin or trypsin removed FPF but heating at 95°C. for 35 minutes at *p*H 2 did not affect FPF or M protein. Absorption and agar diffusion experiments failed to separate M protein from FPF. The addition of hyaluronic acid to a typable culture resulted in loss of FPF activity and probably accounted for the difficulty in demonstrating the factor in the mucoid strains of T18 tested. The similarities and differences between staphylocoagulase and FPF are discussed. *M. Patricia Jevons*

FREIMER, E. H., KRAUSE, R. M. & MCCARTY, M. **Studies of L Forms and Protoplasts of Group A Streptococci. I. Isolation, Growth, and Bacteriologic Characteristics.** *J. Exper. Med.* 1959, Dec. 1, v. 110, No. 6, 853–74, 1 text fig. & 6 figs. on 3 p's. [39 refs.]

When Group A streptococci were grown on agar plates containing 4% sodium chloride and a ditch with 1,000 units per ml. penicillin, small colonies developed within the inhibited zone, resembling the L colonies described previously [this *Bulletin*, 1952, v. 27, 460]. Conversion to the L form was more efficient if salt-tolerant colonies were first selected.

By treating group A streptococci with the enzyme produced in the phage lysis of group C streptococci, in media containing 4% NaCl, the cocci were converted to osmotically-sensitive spherical bodies having the characteristics of protoplasts. Electron microscopy of the debris resulting from the lysis of these protoplasts in water revealed membranes much thinner than typical cell walls. 7% NaCl allowed a better protoplast yield than 4% but even so some streptococci were lysed during preparation. From determinations of the proportion of the original cell DNA liberated during protoplast preparation and subsequent lysis it was estimated that, in 7% NaCl, $\frac{2}{3}$ of the protoplasts remained intact. Practically all the rhamnose of the cell was liberated into solution during protoplast production, as was the M protein.

Colonies of protoplasts could be obtained by inoc lating the suspension, after treatment with the phag associated enzyme, into agar with 4% NaCl; the yie was about 12% of the inoculated cells. The coloni could be transferred to the surface of plates by transf of blocks of agar, but growth in fluid media was n obtained. The protoplasts were resistant to penicilli but sensitive to other antibiotics, except in the case a streptomycin-resistant streptococcus, which yielde streptomycin-resistant protoplasts.

Protoplasts growing in agar plates were shown t produce a haemolysin and deoxyribonuclease; they als produced type-specific M antigen which diffused o into the agar and was able to produce precipitin lin when tested in diffusion plates with type-specific antiser *R. E. O. Williams*

WOOD, Marion. **The Clotting of Rabbit Plasma b Group D Streptococci.** *J. General Microbio* 1959, Oct., v. 21, No. 2, 385–8.

A number of strains of the various biochemica species of group D streptococci were found able to clo citrated rabbit plasma. This was not due to citra utilization, but the strains could not clot plasma con taining 5 units per ml. of heparin, which was readil clotted by staphylococci. Extracellular clotting factc could be obtained by growth within Cellopha membranes in nutrient medium. The nature of th factor was not discovered.

[See also this *Bulletin*, 1953, v. 28, 222.]

R. E. O. Williams

JUNGFER, E. & SCHNEEWEISS, B. Beiträge zur Kultu des *Mycobacterium tuberculosis*. [**Observations o the Cultivation of** *Myco. tuberculosis*] *Ztsch f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 195 July–Aug., v. 5, No. 4, 193–207, 6 figs. (5 on folding pls.) [236 refs.]

An elaborate survey of the literature on growth c the *Myco. tuberculosis* in culture media is presente and reveals that overall most work has been done wit the Tween-Dubos medium but that the egg media c Löwenstein, and of Kirchner and Hohn, have been use almost as much. In Germany the two last are th media which have been most employed.

For a comparative test only a limited number of th many fluid media available were selected. These wer those of Darzin, of Hermann-Kirchner, of Dubos i two modifications and the Proskauer-Beck medium a modified by Youmans.

34 different strains were used of which 8 were bovin one avian and the rest human.

The time interval between inoculation of the mediu and earliest appearance of growth was recorded fc three inocula, the second and third being 100 and 10,00 times less than the first. As the results with the bovin strains presented too many irregularities, comparison were made by taking the average times for first appea ance of growth of all human strains tested.

The outcome of these observations was that th

generation time was found to be on the average distinctly less in Youmans medium. The superiority was most marked with the smallest inoculum but the shortest interval to appearance of growth after heavier inoculation with recently isolated strains was recorded for the 2 media with Tween—those of Dubos and Hauduroy. *J. W. McLeod*

Schneeweiss, B. & Jungfer, E. Beiträge zur Kultur des *Mycobacterium tuberculosis*. II. Mitteilung. [**Observations on the Cultivation of** *Myco. tuberculosis*. **2nd Communication**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete*. Berlin. 1959, Sept.–Oct., v. 5, No. 5, 279–94, 7 figs. (6 on folding pl.) [41 refs.]

With methods described in the previous communication, the average generation time in hours was determined for 6 solid media in common use for the growth of the *Mycobacterium tuberculosis*.

The media used and the generation times recorded were as follows: the bromcresol purple glycerin egg medium of Wagener and Mitscherlich [this *Bulletin*, 1952, v. 27, 479]—26·9 hours (this medium which facilitates differentiation of bovine and human strains since only the latter produce a colour change to yellow due to acid production from glycerin, is extensively used in Germany); Jensen's modification of the Löwenstein medium—20·5 hours; Hohn's egg medium—24·9 hours; Gottsacker's modification of Hohn's medium —27·4 hours; the potato egg medium of Petragnani 34·5 hours; the various albumin and oleic acid agar media of Dubos and his colleagues—27·0 hours.

[It is important, however, that if the results with recently isolated strains only are considered this order is changed and the Dubos medium is best.]

J. W. McLeod

Darzins, E. **Deoxyribonucleic Acid as Growth Stimulant of Tubercle Bacilli.** *Amer. Rev. Respiratory Dis.* 1959, Dec., v. 80, No. 6, 866–70, 4 figs. [11 refs.]

The deoxyribonucleic acid used in this study was obtained from living tubercle bacilli of the H37Rv strain and the Ravenel bovine strain. The bacilli were ground by prolonged shaking with a mixture of glass beads and glass powder suspended in a borate buffer pH 8·1 containing sodium citrate and sodium chloride. After removal of the bacterial debris by centrifuging the fluid was poured into ethanol, the precipitate collected and further purified by treatment with 0·1 M sodium chloride, reprecipitation with ethanol, and treatment with chloroform and *n*-amyl alcohol.

This mode of preparation and the physical and chemical properties [data of these are given] indicated that the substance was pure DNA; it was acid-alcohol-fast and the yield was 0·47% of the original weight of bacilli.

The DNA was added to tubes of fluid basal medium containing Tween 80, in decreasing 10-fold concentrations, starting at 200 μgm./ml. The tubes were then inoculated with a small inoculum of a strain of BCG which had been kept for many months in a refrigerator and which was growing poorly on solid medium. After 8 days' incubation the tube containing 2×10^{-4} μgm./ml. had a heavy growth of ropy tubercle bacilli; the dried weight of this growth was 17 mgm. as compared with 4 mgm. for that of the control tube. Similar stimulation of growth occurred in serum-glycerol-agar with this strain of BCG and with H37Rv. Turbidimetric measurements of the rate of growth indicated that the stimulating effect was due to a shortening of the lag-period. DNA from *Mycobacterium phlei* had only feeble growth enhancing effects on BCG.

The author suggests that this DNA of the tubercle bacilli may be of value for culturing tubercle bacilli from old tuberculous lesions. *S. R. M. Bushby*

Corda, M. L'identificazione del micobatterio tubercolare bovino. [**The Typing of Bovine** *Mycobacterium tuberculosis*] *Ann. Sclavo.* Siena. 1959, Sept.–Oct., v. 1, No. 5, 539–54. [42 refs.] English summary (6 lines).

After reviewing the common criteria on the basis of which *Mycobacterium tuberculosis* is identified as being of the human or bovine type, the author concludes that none of these is of absolute value. Infectivity to various animal species, for example, is not conclusive owing to the occurrence of attenuated strains. He refers to, among others, a recent investigation by G. Meissner (*Tuberkulosearzt*, 1959, v. 13, 74), on 5,000 strains isolated between 1953 and 1957 in Western Germany.

For the identification of a species as belonging to the bovine type, the author says it appears to be enough to carry out the following examinations:

(a) a study of the cultural characteristics with special reference to the stimulating effect or otherwise of glycerol.

(b) the niacin reaction (the production of nicotinic acid in easily determinable quantities) which is positive in the human and negative in the bovine types. This was borne out by work carried out in the tuberculosis clinic of the university of Milan on 22 strains of the bovine type and on 87 strains isolated from human cases. It also appeared that some bovine strains can become niacin positive after cultivation on 4% glycerol medium.

(c) the virulence for rabbits (with 0·01 mgm. intravenously).

(d) the fact that the human type is sensitive to concentrations of kanamycin higher than 10 μgm./ml., while bacteria of the bovine type are generally (though not always) resistant. Human types are quoted as being sensitive to PAS and to thiophenylcarboxylic acid and to furfurol-2-hydrazine, in both cases at concentrations higher than 10 μgm./ml. while the sensitivity of the bovine types varies.

(e) possibly the further study of mycobacteria after they have been recovered from the rabbit.

In spite of this, the author believes in the existence of intermediate types and also thinks there are strains which cannot be typed with certainty. *E. Agius*

PAOLINI, F. A. & MONCALVO, F. Primi dati sperimentali sull'attività catalasica di *Mycobacterium tuberculosis* irradiato. [**First Experimental Results of Studies on the Catalase Activity of Irradiated** *Mycobacterium tuberculosis*] *Ann. Sclavo.* Siena. 1959, Sept.–Oct., v. 1, No. 5, 555–68, 5 figs. [35 refs.] English summary.

The authors studied the changes in catalase activity of *Mycobacterium tuberculosis* following exposure to roentgen radiation, with the dose as the only variable. Radiation was produced by a contact therapy tube of the H 60/6021 type, with the following specifications: 60 Kv, mA 4, 1·5 cm. distance, without filters. The dose varied from 1,000 to 80,000 r. The strains of *Mycobacterium tuberculosis* used were H37Rv, 1 bovine, 1 avian, and 2 " paratuberculosis " strains, 1 of which was streptomycin-resistant. 4 mgm. of bacteria were suspended with the addition of Tween 80 in 1 ml. of normal saline solution, and irradiated in a capsule 5 mm. high and 1·5 cm. in diameter receiving a dose of 1,350 r.p.m. After irradiation suspensions were centrifuged at 1,500 r.p.m. for 20 minutes. Catalase activity was tested by its action on a standard solution of H_2O_2 by estimating residual H_2O_2 after an hour's exposure. For every estimation 4 mgm. of mycobacteria were placed in contact with 0·4 ml. phosphate buffer 0·1 M *p*H 7, 0·2 ml. of 0·3% solution of H_2O_2 being then added. After an hour in the refrigerator at 4°C., 0·5 ml. of a normal solution of H_2SO_4 was added and then, by tenths of a ml. a 1·12% solution of $KMnO_4$, a solution which had been standardized so that, in the absence of bacteria, 1·1 ml. of it would colour the mixture containing 0·2 ml. of 0·3% solution of H_2O_2.

Results showed that the type of radiation used decreases catalase activity proportionately to the dose. Radiations below a certain limit (10,000 r) sometimes produced an increase. Inhibition was only complete in 1 out of 5 cases, a small degree of activity persisting even after doses which had been enough to affect the vitality of the mycobacteria. Sensitivity of the same enzyme varies in the different strains, but is constant for the same strain, other conditions remaining the same. The strain in which complete abolition followed the use of 60,000 r was a streptomycin resistant one and the authors surmise that the character of antibiotic resistance may be linked with changes in the enzyme systems making them more sensitive. The work confirms that roentgen radiation is capable of producing early and considerable functional biochemical changes.

E. Agius

UYEDA, C. T. & RAFFEL, S. **Virulence of the Tubercle Bacillus. III. Effect of Penicillin upon the Growth of Virulent and Avirulent Bacilli.** *Amer. Rev. Respiratory Dis.* 1959, Dec., v. 80, No. 6, 849–54, 3 figs. [27 refs.]

The sensitivity of 5 virulent strains, 2 attenuated strains and 4 avirulent strains of tubercle bacilli to penicillin G was determined in Dubos oleic-acid-albumin liquid and agar media. The effects were assessed by the reduction of the turbidity of the fluid culture and on the number of colonies growing on the soli medium.

4 of the virulent strains were fully resistant to 100 200 units of penicillin per ml. and the 5th strain wa completely resistant to 50 units/ml. but not to 10 units/ml. The 2 attenuated strains (R1Rv and BCG were sensitive to 200 units/ml. and only partially resistant to 50 units/ml. 1 of the avirulent strains (H37Ra was intermediate in resistance between the virulent an the attenuated strains and the other 3 were relativel sensitive to the antibiotic, 2 being partially inhibite by 1–2 units/ml. These differences in susceptibilit were more apparent after 2 weeks' incubation than afte 6 weeks.

These results obviously have important implication where penicillin is used to suppress the growth of con taminants, especially when avirulent strains are bein grown.

[For earlier parts, see this *Bulletin*, 1954, v. 29, 872

S. R. M. Bushby

DURR, F. E., SMITH, D. W. & ALTMAN, D. P. **A Comparison of the Virulence of Various Known an Atypical Mycobacteria for Chickens, Guine Pigs, Hamsters, and Mice.** *Amer. Rev. Respirc tory Dis.* 1959, Dec., v. 80, No. 6, 876–85, 2 figs [16 refs.]

This interest of the authors in evaluating the virulenc of atypical acid-fast bacilli arose from the similarit of the growth of avian tubercle bacilli and that of th non-photochromogens on ATS egg medium, and from the facts that both of these bacilli are resistant t mycobacteriophage and contain a common specifi glycolipid-peptide, " Jav ".

The 4 species of animals used in this study wer injected with the various mycobacteria growing i Dubos medium; the chickens were infected sub cutaneously or intravenously, the guineapigs subcutane ously, the hamsters intraperitoneally and the mic intravenously. The inocula used ranged from 10^5–1 viable units.

The 4 strains of photochromogens produced very litt disease in the chickens and guineapigs, but extensiv disease in the hamsters and mice. Only 1 of the strains of non-photochromogens was tested in all th test animals and this strain produced no lesions; 2 c the other strains produced small granulomas in th chicken.

The avian tubercle bacilli caused some degree c disease in all of the animals but in the hamsters an mice it was less than that produced by the photo chromogens; the lesions produced in the chicken b the 9 strains tested were extensive and they were thu in marked contrast to the minimal lesions produced b the atypical acid-fast bacilli.

The strain of human tubercle bacillus used produce extensive disease in the guineapig and the hamster bu only moderate disease in the mouse and none in th chicken. The 2 saprophytes, *Mycobacterium phlei* an *Myco. smegmatis*, produced no lesions in any of th animals, although the second organism was recovere from the spleens of some of the mice and guineapigs.

These results suggest that if the non-photochromogens are related to virulent avian tubercle bacilli, then they must be very attenuated strains. *S. R. M. Bushby*

RAPAPORT, F. T. & MILLAR, J. W. **Failure to transfer Delayed Tuberculin Sensitivity from Human to Animal Species.** *Proc. Soc. Exper. Biol. & Med.* 1959, Dec., v. 102, No. 3, 714–17.

"This report describes attempts to transfer delayed sensitivity to tuberculin to monkeys and to rabbits by means of peripheral blood leucocytes obtained from sensitive human donors. No such transfers were obtained."

WILLIAMS, C. A., Jr. & DUBOS, R. J. **Studies on Fractions of Methanol Extracts of Tubercle Bacilli. I Fractions which increase Resistance to Infection.** *J. Exper. Med.* 1959, Dec. 1, v. 110, No. 6, 981–1004, 7 figs. [34 refs.]

This lengthy paper describes in detail the procedures used in obtaining at 60°C. the methanol extract from heat-killed tubercle bacilli and in its sub-fractionation. Briefly, the sub-fractionation was accomplished by concentrating the extract at 45–50°C., and collecting the various components as they reached their critical concentration. The first 2 components, F I and F II, were further refined, and F I was shown to be insoluble in petrol-ether and F II to be soluble in this solvent. F I was further fractionated by treatment with either ethanolic salt solutions to yield F I-P, which consisted of 50% carbohydrate, and F I-S, which had not been analysed, or by titration with cupric acetate to yield F I-CP or F I-CS (P = precipitate; S = supernatant).

The immunizing activities of these extracts were compared by injecting the extracts intraperitoneally into mice and later challenging the mice by the intravenous injection of bovine tubercle bacilli. Analysis of the results showed that F I gave slight protection but its 2 sub-fractions, F I-S and F I-CS, gave greater protection. F II gave slightly greater protection than F I but the highest protection was given by a mixture of F I and F II. The results of an experiment, designed to establish the relationship between the degree of immunity and the time interval between vaccination and challenge, indicated that there was a maximum response at 2 weeks followed by a fall at 4 weeks, rising again at the 8th and 12th weeks. In experiments in which staphylococci were used as the challenge organisms, some protection was afforded, and this was highest at the end of the 2nd week, falling to a low level by the 4th week and not rising again.

In the lengthy discussion the authors suggest that F II acts as an adjuvant increasing the immunological response to F I. They also suggest that the first immune response is one of "broad-specificity" due to an antigen common to the tubercle bacillus and the staphylococcus, whereas the second immune response is due to stimulation of a more specific and longer sustained mechanism.

[Details of the physical and chemical properties of these fractions are to be published elsewhere.]

S. R. M. Bushby

KOCH, Marie L. & KROLL, A. W. **An Investigation of the Reliability of the Niacin Test, the Neutral Red Test, and the Test for Cord Formation for Differentiation of Group III ("Battey" Strains) of Atypical Mycobacteria from Human Tubercle Bacilli.** *Amer. Rev. Respiratory Dis.* 1960, Jan., v. 81, No. 1, 108–10. [10 refs.]

"Of the three laboratory procedures investigated for differentiating between *Group III* atypical mycobacteria and virulent human tubercle bacilli, only the test for demonstration of 'serpentine' cord formation proved of value. Results of the direct test for niacin production were too inconsistent to warrant the use of this test for the above-stated purpose, and both types of acid-fast bacilli were able to bind the dye neutral red."

ROSS, A. J. *Mycobacterium salmoniphilum* **sp. nov. from Salmonoid Fishes.** *Amer. Rev. Respiratory Dis.* 1960, Feb., v. 81, No. 2, 241–50, 28 figs. [23 refs.]

JUHASZ, S. E. **Interspecific Hybridization among Mycobacteria.** [Correspondence.] *Nature.* 1960, Jan. 23, v. 185, 265.

JENEY, E. & ZSOLNAI, T. Versuche zur Entdeckung neuer Tuberkulostatika. IX. Die mit verschiedenen Aldehyden und Ketonengebildeten Derivate von Mandelsäure-hydrazid. [**Attempts to find new Tuberculostatics. IX. Compounds of Mandelic Acid Hydrazid and different Aldehydes and Ketones**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 2, 215–19. X. Amino-triazine und Amino-triazole. [**X. Amino-Triazin and Amino-Triazole**] *Ibid.*, 220–29. [18 refs.]

The English summaries appended to the paper are as follows:—

ix) "The authors synthesized compounds of mandelic acid and fifteen substances containing one or more carbonyl groups. The tuberculostatic action of these compounds and of mandelic acid hydrazid tested in vitro, proved to be only of a low one. The authors do not ascribe a specific action to these compounds."

x) "The authors produced 30 compounds, 5 of which were derivates of 1, 3, 5-triazin, 5 were derivates of 1, 3, 4-triazol, 4 were imidazol-derivates. 8 substances can be assumed as more or less structurally related compounds.

"The bacteriostatic and fungistatic effect of these compounds was examined. Only 7 of them exercised a noticeable tuberculostatic effect. Only three substances had an effect upon the apathogenic acid-resistant bacteria, 5 substances upon the gram-positive bacteria. Only 1 substance had a propagation-inhibiting effect upon fungi strains.

"The authors conclude, that the effect intensity of the 30 compounds and also of the 7 substances mentioned afore with a marked tuberculostatic effect is not strong enough to permit the assumption of a specific mechanism of effect."

McFadzean, J. A. & Valentine, R. C. **The Examination and the Determination of the Viability of** *Mycobacterium leprae* **by Electronmicroscopy.** *Leprosy Review.* 1960, Jan., v. 31, No. 1, 6–11, 4 figs. on 2 pls.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1960, v. 57, 481.]

Romanov, G. V. **Dried Phosphate-Peptone Agar for Determining the Toxigenicity of Strains of** *Corynebacterium diphtheriae. J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 12, 1899–904. [Translated from Russian.]

This paper, which deals with the production of a dried phosphate peptone agar for the determination of diphtheria toxin production by the gel diffusion test, brings out some important theoretical points bearing on such tests.

The peptone used in preparing this medium was Marten's [? Martin's] and it is emphasized that in order that this product should be satisfactory it must be sufficiently hydrolysed in the preliminary pepsin digestion to have lost viscosity as tested by free running from a glass rod lifted from the liquid after stirring, the absence of viscosity in the last drops flowing from the rod being a satisfactory indication.

The digested material, which is inactivated at 80°C. for 10 minutes, is left to stand for 10–12 days in a refrigerator at 6–8°C. The supernatant is then decanted, filtered through cotton wool, and, after heating to 80°C. is brought to *p*H 8–8·2 with 10% caustic soda and boiled for 10 minutes. At this stage a 5 ml. filtered sample of the product so obtained should remain clear after the addition of 2 drops of 10% caustic soda. Finally, the hydrolysate is filtered through tightly packed cotton wool at 60°C.

Only such preparations are suitable for the preparation of a phosphate agar which will give satisfactory lines of precipitation independently of the addition of serum. The dried agar which was first prepared was not, however, found suitable. An investigation of the underlying cause led to the establishment of the following points:—

Proteins of high molecular weight appear to absorb iron readily and the value of the addition of serum to a medium depends on its capacity to absorb iron on the one hand and to liberate iron on the other. In this respect serum acts as a buffer in media used for diphtheria toxin production for diffusion tests and, within certain limits only, will yield sufficient iron to a medium which is deficient in that substance or take up and neutralize iron present in excess.

If a serum tinted with dissolved haemoglobin and hence rich in organic iron is used, however, no satisfactory toxin/antitoxin lines are obtained. Finally, the faults in the dried preparations of the phosphate agar were traced to the absorption of iron from the apparatus used for drying and a perfectly satisfactory product could be obtained from apparatus made from stainless steel.

The addition of serum to such agar may well be o value insofar as it may buffer the medium so as t adapt it to the varying iron requirements of th different strains. *J. W. McLeod*

Simonetti, N. Sull'azione biologica dei corpi batteric di *C. diphtheriae.* [**Effect of the Bacterial Cell of** *C. diphtheriae* **on the Animal Body**] *Nuovi Ann d'Igiene e Microbiol.* 1959, May–June, v. 10, No 3, 253–65. [104 refs.] English summary (7 lines).

In view of the conflict of opinion as to the effec of factors other than the classical neurotoxin in th production of diphtheria, the effect of injecting bacteri free from toxin was investigated on the guineapig an rabbit. The vaccines were prepared by growing th *Corynebacterium diphtheriae* in presence of excess c Fe and subsequent exposure to 1% formaldehyde fo periods of 20 or 40 days.

The test doses of living bacteria were also prepare from cultures devoid of toxin.

Animals vaccinated in this way resisted a fatal dos of bacteria considerably longer than the controls an sometimes survived. No antitoxin could be demon strated in their sera and they were more rather tha less sensitive to injections of toxin.

It is concluded that the increased resistance was du to factors other than antitoxin and was more probabl explained by phenomena of hypersensitivity leading t increased local reaction at the site of injection of th test dose of bacteria. *J. W. McLeod*

Penso, G. & Vicari, G. Studio dei fenomeni immun tari per mezzo delle colture di tessuto. VIII. Tito lazione del'a tossina e dell'antitossina difteric [**Studies of the Immune Phenomena by Tissu Culture Technique. VIII. The Titration of Diph theria Toxin and Antitoxin**] *Rendiconti Istitut Superiore di Sanità.* Rome. 1959, v. 22, Pt. 516–25, 2 figs. [10 refs.] English summary lines).

The method adopted for titration of the activity toxin was to use the cells of the tissue culture K which grow rapidly in media containing a low pe centage of serum and were grown in a medium consistin of Hanks solution 85 parts, 5% hydrolysate lactalbumin 5 parts and inactivated calf serum 10 part A cell suspension spun out from such cultures and co taining about 200,000 cells/ml. was prepared in th same medium. Mixtures of progressive dilutions toxin in Hanks solution 0·5 ml., of cell suspensio 0·5 ml. and of 1 ml. of the nutrient medium we incubated for 4 days in presence of phenol red indicat and the life or death of the cells was determined as the "metabolic method" of Salk *et al.* [this *Bulleti* 1955, v. 30, 184] by absence or presence of colo change from rose to lemon yellow.

The degree of toxic action was determined by th diminution of colour change and the delay in i

initiation as compared with the change in the control without toxin.

Details are given of the method of adopting these observations to the titration of antitoxin. It was found possible to determine 1/50 of a standard unit of antitoxin by this method.

It is claimed that the method is more sensitive than the original method of EHRLICH and much less difficult in execution than that of JENSEN.

Both of these methods are more expensive on account of the use of animals and that of Jensen troublesome because of the requirement of a special strain of rabbit not easily bred and acclimatized in different parts of the world.

In respect of simplicity, low cost and reliability, therefore, the method described is claimed to be the best method available for routine titrations of diphtheria toxin and antitoxin.

Observations on the effect of toxin on the respiration of culture cells by Warburg's technique showed that, although larger doses of toxin markedly inhibited the uptake of O_2, lesser doses might cause it to exceed that of the control. *J. W. McLeod*

ROWLEY, D. A., CHUTKOW, J. & ATTIG, C. **Severe Active Cutaneous Hypersensitivity in the Rat produced by *Hemophilus pertussis* Vaccine.** *J. Exper. Med.* 1959, Nov. 1, v. 110, No. 5, 751–70, 5 text figs. & 5 figs. on 2 pls. [17 refs.]

Haemophilus pertussis vaccine injected into normal rat skin produced local oedema which soon subsided and which was followed 4 to 6 days later by severe inflammation at the site of injection. This is called the primary hypersensitivity response. When the injected skin of the sensitized animal was challenged 5 to 28 days after the initial injection, severe inflammation developed at the site of challenge within 12 to 24 hours. This is called the secondary hypersensitive response which was induced by a dose of vaccine causing little or no initial or delayed inflammation in a normal rat.

Specific cutaneous hypersensitivity to either a particulate antigen (such as typhoid vaccine) or a soluble antigen (human or rabbit gamma globulin) developed when rats were injected with a mixture of the antigen and pertussis vaccine.

Cutaneous hypersensitivity to pertussis vaccine was passively transferred to normal rats by lymph node cells but not by serum from hypersensitive rats. Sensitization with pertussis vaccine did not enhance the oedema-producing activity of histamine, serotonin, or 48/80 (a powerful histamine release agent) given subcutaneously. Mast cells in areas of hypersensitive inflammation were not damaged appreciably.

The authors believe that their studies have failed to demonstrate a role for circulating antibody in the cutaneous hypersensitive inflammation induced in the rat by pertussis vaccine and the inflammation is not mediated by serotonin or histamine or both.

F. T. Perkins

ANDERSEN, Else K. & BENTZON, M. W. **The Failure to show Correlation between Type-Specificity and Protection in Experimental Pertussis in Mice. (Sublethal Intranasal Challenge.)** *Acta Path. et Microb. Scandinavica.* 1958, v. 43, No. 1, 106–12, 1 fig.

Using a sublethal intranasal challenge dose of *Bordetella* [*Haemophilus*] *pertussis* organisms in mice immunized by a single intraperitoneal dose of vaccine the authors showed that the protective effect of the vaccine appeared to depend upon the strain of organisms used for challenge. Mice immunized with a vaccine prepared from the challenge strain of organisms were not able to withstand challenge any better than were mice immunized with a heterologous strain. No correlation between type-specificity and protection could be demonstrated. *F. T. Perkins*

KUWAJIMA, Y., MATSUI, T., NAKA, K. & KANAI, Y. **Inability of Pertussis Toxin to act as Preventive Antigen in Experimental Mouse Infection of *Bordetella pertussis*.** *Osaka City Med. J.* 1958, Jan., v. 4, No. 2, 177–88, 3 figs. [22 refs.]

The authors used a particular strain of *Bordetella* [*Haemophilus*] *pertussis* (no. 33) which by their tests was shown to be extremely toxic, to have a thermolabile antigen in addition to the L-antigen of phase-1 organisms and to be devoid of phase-1 S-antigen. Both the living organisms or extracted toxin produced high titre antitoxin in rabbits. Active or passive immunization of mice with the organisms or antisera produced to them was unable to protect mice against an intracerebral pertussis challenge although the organisms induced histamine sensitization in the mouse.

F. T. Perkins

MACLENNAN, A. P. **Specific Lipopolysaccharides of *Bordetella*.** *Biochem. J.* 1960, Feb., v. 74, No. 2, 398–409, 8 figs. [63 refs.]

EWING, W. H. & EDWARDS, P. R. **The Principal Divisions and Groups of Enterobacteriaceae and their Differentiation.** *Internat. Bull. Bact. Nomencl. & Taxon.* 1960, Jan. 15, v. 10, No. 1, 1–12. [19 refs.]

In this paper the authors do not attempt to present a review of previous classifications or different systems of nomenclature. Instead, they describe an essentially practical diagnostic scheme which they have used and taught over many years [and a very useful scheme it is].

The family is divided into 4 "Divisions", each containing two or more of the "Groups" recognized by the Enterobacteriaceae Subcommittee of the International Nomenclature Committee.

The authors [wisely in the opinion of the abstracter] avoid all issues of nomenclature and use the common names of the different groups. [The use of the name Aerobacter may cause some confusion; Aerobacter as used in this paper refers to the genus as redefined by HORMAECHE and EDWARDS [this *Bulletin*, 1958, v. 33,

979], and consists of motile rods with IMViC reactions −− ++, and corresponds to the group labelled Cloaca (Aerobacter) in the Subcommittee's Report [*ibid.*, 507].

In discussing these Divisions the "paracolon" group does not have a place for, as the authors point out, there is no such thing as "a paracolon group". The term paracolon has lost its original meaning, that of an organism that fermented lactose slowly. Each group of bacteria that ferments lactose rapidly (*e.g. E. coli*) also contains members in which lactose fermentation is slower or even may be negative.

The paper contains 8 tables of characters by which the members of the different groups can be distinguished; these tables will be invaluable to all enterobacteriologists.

S. T. Cowan

ANDREYEVA, G. V. **A Molybdenum Medium for detecting and identifying Bacteria of the Enteric Group.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 2, 86–90. [11 refs.] [Translated from Russian.]

Media for distinguishing between different organisms often include chemical indicators to show changes in *p*H value following fermentation or deamination. The author of this paper describes the principles of a complex medium for which he claims that colour changes are indicative of changes of both oxidation-reduction potential and *p*H value, and by which different members of the enteric bacteria can be distinguished.

The medium has as its base a meat peptone agar prepared with Hottinger broth [not described]; to the base is added 0·4% ammonium molybdate, 1% lactose, 1% glycerol, an unspecified amount of sodium sulphite, 1% urea, 0·2–5 [presumably 0·2–0·5]% alcoholic fuchsin, and *p*H adjusted to 7·2. On this medium coloured colonies can be seen and identified after 10 hours incubation.

Blue colonies	=	*Escherichia coli*
Yellow	=	*Aerobacter aerogenes* *Shigella sonnei* Paracolobactrum [Hafnia]
Pink (transparent)	=	*Shigella flexneri*
Pinkish-yellow	=	*Salmonella typhi* *Salm. paratyphi*—A and B
Bright pink	=	*Alcaligenes faecalis* *Proteus morganii* *Proteus vulgaris*

S. T. Cowan

SMITH, H. G. **Observations on the Isolation of Salmonellae from Selenite Broth.** *J. Applied Bact.* 1959, Apr., v. 22, No. 1, 116–24, 4 figs.

A study of the growth curves of various salmonellae in selenite broth showed that they grew more luxuriantly in the presence of a fermentable carbohydrate. After the peak growth, however, there was generally a sharp decline with the reduction of the selenite to selenium. The reduction to selenium which affects the growth curves is related to the presence in the medium of a fermentable carbohydrate. In mixed cultures the presence of a carbohydrate whic is utilizable by one member may result in condition which will affect the growth curve of another membe not using this particular carbohydrate. For instanc with a mixed culture containing *Citrobacter freund* and *Salmonella typhi-murium* grown in lactose seleni broth the advantage was all with *Cit. freundii*, eve with mannitol in place of lactose some advantage la with this organism; only when selenite broth, witho added carbohydrate, was used were the growth curv of the 2 organisms of the same order.

When, however, comparative tests were undertake with different selective media on routine specimens faeces selenite broth proved to be an efficient pr liminary selective medium. Used with MacConkey ag the results were good, but they were even better wh it was combined with deoxycholate-citrate agar. Th selectivity of selenite broth appeared to be improv by the addition of gentian violet. The same auth has recently studied the nature of the selective actio of selenite broth [see this *Bulletin*, 1960, v. 35, 188].

The value of selenite broth as an enrichment mediu for the routine isolation of salmonellae from faec specimens is generally accepted, but there are ma factors that control its selectivity: the original mediu from which the organism is cultivated, the growth pha of the organism itself, its proportionate representati in the mixed flora (which is generally unknown routine material) and the culture time in the enric ment medium; in addition to other growth factors s out in the author's companion paper [*loc. cit.*]. T comparative studies do not include other enrichme media.

H. J. Benstead

SALMON, J. Constitution antigénique des lysats Salmonella Schottmuelleri. [**Antigenic Constit tion of Lysates of** *Salmonella paratyphi B*] *Re Belge Path. et Méd. Expér.* 1957, Oct., v. 26, N 3, 191–211, 4 figs. [46 refs.]

Schottmüller's bacillus is more generally known the paratyphoid B bacillus and this particular pap is concerned with electrophoretic and serologi studies of various lysates, prepared with differe reagents, of this organism for the recognition of certa chemical and antigenic fractions; they include identification of the proteins, lipids and the gly proteins and the recognition of the number of differe antigen fractions.

The various lysates were prepared from the sa strain of *Salmonella paratyphi B* by treating suspensi of bacterial cells containing approximately 10^9 via bacteria per ml. with glycine, glycine plus pyroph phate, pyrophosphate and orthophosphate respectiv Mycolysates of both living and killed bacterial ce produced by the action of "actinomycin", were a used.

The autolysates obtained with glycine, glyci pyrophosphate and pyrophosphate alone all contai proteins in significant quantity and the electrophoro picture was identical in each case. The lysates orthophosphate were, however, poor in protein.

Antisera were prepared in rabbits against the 6 lysa and it was found that each lysate exhibited a distinct

reaction-pattern to homologous and heterologous antisera when examined by bacterial agglutination, precipitation in liquid and agar-gel techniques and in immuno-electrophoresis. 6 antigens, *a*, *b*, *c*, *d*, *e*, and *f* in all were identified and antigen *b* was recognized in 5 of the 6 lysates. No lysate contained all the 6 antigens, but the glycine-pyrophosphate lysate contained 4. All lysates induced the development of precipitins in the rabbit, but agglutinins were found only in those animals injected with glycine, glycine-pyrophosphate, pyrophosphate and orthophosphate lysates. Anti-mycolysate sera failed to show any bacterial agglutinins.

H. J. Bensted

TANAKA, N., NISHIMURA, T. & YOSHIYUKI, T. **Histochemical Studies on the Cellular Distribution of Endotoxin of** *Salmonella enteritidis* **in Mouse Tissues.** *Japanese J. Microbiol.* 1959, Apr., v. 3, No. 2, 191–201, 8 figs. (6 on pl.) [10 refs.]

JONK, Leonie & SCHRIRE, L. **Salmonella Haddon—A New Serotype.** *South African J. Med. Sci.* 1959, July, v. 24, Nos. 1/2, 3.

"A description is given of a new Salmonella serotype, S. haddon $(16:z_4,z_{23}:-)$."

OLARTE, J., GALINDO, Emma & FORMAL, S. B. **Serotypes of** *Shigella flexneri* **found in Children in Mexico City.** *Bol. Oficina Sanitaria Panamericana.* 1959, Dec., v. 47, No. 6, 507–8.

"A survey was made to determine the distribution of *Shigella flexneri* serotypes in Mexican children with gastroenteritis. Out of a total of 159 strains of *Sh. flexneri* that were isolated, 85 (53 per cent) were *Sh. flexneri* 2a. The possible epidemiological significance of this finding is discussed."

DIXON, J. M. S. **Observations on the Growth in Nutrient Broth of Mixtures of** *Escherichia coli* **Strains, and of Faecal Specimens harbouring Pathogenic** *Escherichia coli* **Serotypes.** *J. Hygiene.* 1959, June, v. 57, No. 2, 174–83.

This paper describes a series of experiments designed to discover whether or not nutrient broth could be used as an enrichment medium for pathogenic strains of *Escherichia coli*. Experiments with laboratory cultures indicated that when nutrient broth was inoculated with widely different numbers of 2 or more strains and then incubated, the strains tended to equate, and that this tendency increased with the length of incubation. One random example is that of an inoculum consisting of 2 strains in the ratio of 1:100,000; this ratio was reduced to 1:135 after 18 hours incubation and to 1:10 after 168 hours. These experimental results were applied to a field trial, and it was found that nutrient broth incubated at 44°C. for 24 hours was of value when used in addition to direct plating; when used alone, some "positives" were lost by broth culture. It is suggested that this method of broth enrichment could be of value when screening infant carriers of pathogenic strains of *E. coli*. [See also THOMSON, this *Bulletin*, 1956, v. 31, 446.]

John S. Stevenson

RICKENBERG, H. V. **Role of the Inducer in the Induced Synthesis of β-Galactosidase in** *Escherichia coli*. [Correspondence.] *Nature.* 1960, Jan. 23, v. 185, 240–41, 2 figs. [12 refs.]

REEVES, P. **Role of Hfr Mutants in F+ × F− Crosses in** *Escherichia Coli* **K12.** [Correspondence.] *Nature.* 1960, Jan. 23, 265–6.

IIJIMA, T. & HAGIWARA, A. **Mutagenic Action of Mitomycin** *C* **on** *Escherichia coli*. [Correspondence.] *Nature.* 1960, Feb., 6, v. 185, 395–6.

HALL, A. N., LEESON, J. A., RYDON. H. N. & TWEDDLE, J. C. **The Degradation of some** *Bz*-**Substituted Tryptophans by** *Escherichia coli* **Tryptophanase.** *Biochem. J.* 1960, Feb., v. 74, No. 2, 209–16, 1 fig. [44 refs.]

SMITH, C. H. **Acid-Soluble Nucleotides of Penicillin-Induced Protoplasts of** *Escherichia Coli*. *Yale J. Biol. & Med.* 1959, Nov., v. 32, No. 2, 109–19, 2 figs. [23 refs.]

DEAN, A. C. R. & HINSHELWOOD, C. **Variations in the Nucleic Acid Content of** *Bact. lactis aerogenes* **during the Growth Cycle.** *Proc. Roy. Soc.* Ser. B. 1960, Feb. 2, v. 151, No. 944, 348–63, 9 figs. [35 refs.]

"During the growth cycle of *Bact. lactis aerogenes* in a medium containing glucose and inorganic salts the ratio RNA/DNA rises steeply to a maximum and declines. The variation is due in the main to the RNA. It depends on a complex set of factors affecting the environment, and is not primarily a question of the number of divisions undergone by the original inoculum."

EDWARDS, P. R., FIFE, Mary A. & RAMSEY, Carolyn H. **Studies on the Arizona Group of** *Enterobacteriaceae*. *Bact. Reviews.* 1959, Dec., v. 23, No. 4, 155–74. [39 refs.]

The distinction between the Salmonella and Arizona groups is based on differences in characters shown in the table.

	Salmonella	Arizona
Gelatin	−	+ (slow)
Lactose	−	+ or late +
Dulcitol	+	−
D-tartrate	+	−
Malonate	−	+

Most strains are easy to place by these characters, and only 25 of 30,000 cultures of the 2 groups were difficult. No difficulty was experienced in distinguishing Arizona from Citrobacter except in Arizona O group 21 in which all strains were KCN positive; only 3·3% of other Arizonas were + in the KCN test.

The original strains were isolated from reptiles, and subsequently strains have been isolated from fowls and mammals, including man.

A serological scheme was worked out on cultures collected over 20 years, mostly isolated in the U.S.A. 32 groups are recognized by different O antigens, and 3 are divided into subgroups. Most of the O antigens are related to or are identical with Salmonella O antigens. 36 different H antigens are recognized, and of these 20 are strongly related to Salmonella H antigens; like Salmonellas, Arizona strains may be multiphasic. Tables are given to show strains used for immunization and absorption to make monospecific O and H factor sera. Among 2,634 cultures, 180 antigenic combinations or serotypes were found; 229 of the strains (159 different outbreaks) were from man.

Over the years the prevalence of the different serotypes has changed. Types that were once common almost disappeared when infected turkey hatcheries cleared their stocks. Serotypes 7:1, 2, 6 has increased from 4 in 1947 to 473 when the paper was written, and of these 98 strains were from man. Serotype 7:1, 7, 8 is now being found more often and has been found to infect man.

The use of lactose-containing differential media is responsible for the failure to isolate rapid lactose-fermenting strains, and the frequency of Arizona in man may be much greater than has been recognized.

S. T. Cowan

v. Sprockhoff, H. Über die Inkonstanz des Melitensistyps der Gattung *Brucella.* [**On the Instability of *melitensis* Type of the Genus *Brucella***] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 177, No. 2, 186–95. [17 refs.]

The English summary appended to the paper is as follows:—

"1. Four melitensis strains were subcultured frequently. With one of these strains several passages in guinea pigs and chick embryos were performed. Subcultures of these strains were submitted to agglutination reactions with monovalent abortus viz. melitensis immune sera. Their ability to produce H_2S was tested.

"2. The 'Kützle' strain showed an antigenic variation towards the abortus antigen. The time of this variation could not be determined exactly, since the strain showed this variation already, before the experiments started. The three other melitensis strains had not changed their antigenic structure.

"3. The four melitensis strains tested produced more or less great amounts of H_2S, though the cultures did not do so immediately after their isolation.

"4. The demonstrated variability of serological and biochemical properties shows once again the instability of the melitensis type of the genu Brucella."

Heckly, R. J., Faunce, K., Jr. & Elberg, S. S. **Lyo philization of** *Brucella melitensis. Applied Micro biol.* Baltimore. 1960, Jan., v. 8, No. 1, 52–4 3 figs.

"Survival of cultures of a vaccine strain of *Brucell melitensis* (Rev 1-S) to which equal volumes of 6 pe cent solutions of lactose, sucrose, or glucose had bee added was comparable when tested immediately afte lyophilization. However, after 125 days of storage a room temperature, the viability of the culture wit glucose was markedly less than that of cultures con taining either lactose or sucrose.

"At 0 C there was no loss of viability of culture lyophilized with sucrose after storage for 225 days, bu at room temperature only 0.1 per cent survived, an at 37 C less than 10^{-4} per cent of the cells remaine viable. In no instance was there a significant chang in the ratio of smooth to nonsmooth colonial types.

"Although neither the freezing nor the dryin method affected viability when tested immediately afte lyophilization, viability was best maintained in culture which were snap frozen and dried at about −18C."

Olsufiev, N. G., Emelyanova, O. S. & Dunayeva T. N. **Comparative Study of Strains of *A tularense* in the Old and New World and thei Taxonomy.** *J. Hyg., Epidemiol., Microbiol. Immunol.* Prague. 1959, v. 3, No. 2, 138–4 [Numerous refs.]

When the standard virulent strain of *Brucella tul rensis*, maintained in the U.S.S.R., was compared wi a similar standard strain obtained from the U.S.A. was found that the latter was very much more virulen for rabbits. The rabbit LD100 for the U.S.S.R. strai (No. 503) was 10^9 (one milliard), whereas the rabb LD100 for the American strain (Schu) was only or bacterial cell. Tests with white rats, white mice an guineapigs also showed marked differences in virulenc but they were not nearly so clear cut as the exper ments with the rabbits. Other strains isolated U.S.S.R., and from areas in Eastern Europe and As from tularaemia infections were also found to be muc less virulent for rabbits than strains from the Ne World. It was found that most of the New Wor strains of *Br. tularensis* fermented glycerol whereas th U.S.S.R. strains did not.

The authors did not agree with the inclusion of th organism within the *Brucella* group and they sugge that it should be placed in a group of its own an in recognition of the contributions of Edward Franc to our knowledge of this infection, that it should b given the generic name *Francisella.* Thus the full nam of the U.S.A. standard strain would be:—

Francisella tularensis tularensis, MacCoy an Chapin,

while the U.S.S.R. strain would be given the name:

Francisella tularensis palaearctica, Ols, Emel an Dun.

H. J. Bensted

FULTHORPE, A. J. **Factors influencing Haemagglutination Tests with Tetanus Antitoxin.** *Immunology.* Oxford. 1959, Apr., v. 2, No. 2, 104–11, 2 figs.

The author discusses the results obtained in titrating the antibody content of antitetanic serum by agglutination of sheep red cells coated with toxoid and especially the test of inhibition of such agglutination by toxin-antitoxin mixtures. The titres observed in such tests are found to vary with the concentration of sheep cells used, with the amount of specific antigen that they carry, with the length of time that the toxin-antitoxin mixtures are left to stand before the toxoid-loaded sheep cells are added and with the level of concentration of antitoxin adopted for the test, *i.e.* an LA, LA/10 or LA/100 level.

By using prepared cells of high sensitivity it is possible to get agglutination in toxin-antitoxin mixtures in which there is no excess of antitoxin, the mixtures being in fact lethal in animal test.

On fractionating antisera it was found that the gamma globulin had greater agglutinating effect relatively to its neutralizing action as tested against international standard serum than had the alpha and beta globulin fractions. This was more marked in the sera of horses subjected to one course of immunization than in those which had had many.

The need for carefully standardized conditions in utilizing the test of inhibition of agglutination of sheep cells coated with toxoid in antitoxin titration is emphasized. *J. W. McLeod*

MEYER, E. A. & LAMANNA, C. **Activity of Type A Botulinal Toxin and Hemagglutinin exposed to Proteolytic Enzyme.** *J. Bacteriology.* 1959, Aug., v. 78, No. 2, 175–80. [20 refs.]

The effect of a wide range of digestive enzymes on type A botulinal toxin has shown that the constituent of the toxin responsible for haemagglutination, which is distinct from that giving rise to neurotoxic phenomena, is resistant to those enzymes which destroy the latter. The enzymes found to be destructive of neurotoxin were trypsin, chymotrypsin, ficin as well as two of bacterial origin, the amino peptidase of *Clostridium botulinum* type B and the glutamyl transferase of *Bacillus subtilis.* Pepsin and papain were not found to be active, however.

It is suggested that the apparent anomaly of a toxin sensitive to destruction by trypsin and producing its effect after absorption from the intestine is resolved by the relatively slow tryptic destruction which could be expected to allow of lethal absorption before digestion was completed. *J. W. McLeod*

DUKALOV, I. A. & GOLOSNITSKII, A. K. **The *in vivo* Diagnosis of Botulism.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 12, 1917–21. [Translated from Russian.]

Use was made of a *Cl. botulinum* type B which had an MLD of 0·00001 ml. if administered subcutaneously to the guineapig and 4–8 ml. if administered to the horse by the stomach. Investigation of the horse blood at various intervals after inoculation showed a marked depression of the phagocytic index of the blood for staphylococci 5 hours after injection. The same sample of blood produced characteristic death in the guineapig much later, *i.e.* after several days. The possible value of such an observation depends on the fact that it appears considerably earlier than the development of symptoms in the animal poisoned.

It is admitted that such a reaction is not necessarily specific to this type of infection.

[Presumably neutralization of the inhibitory effect on phagocytosis by appropriate antiserum would render the test specific. This last point is not discussed, however, in the translation of the Russian paper.]

J. W. McLeod

REISS-GUTFREUND, Ruth J. Culture de *Borrelia recurrentis* (souches éthiopiennes) en oeuf fécondé de poule. [**Culture of *Borrelia recurrentis* (Ethiopian Strains) in Fertilized Eggs**] *Ann. Inst. Pasteur.* 1960, Jan., v. 98, No. 1, 131–6. [11 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1960, v. 57, 478.]

EIDMANN, E., LIPPELT, H. & POESPODIHARDJO, S. Quantitative Untersuchungen über die Vermehrung von *Borrelia erratici* in der weissen Maus. [**Quantitative Studies on the Multiplication of *Borrelia erratici* in White Mice**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1959, Nov., v. 10, No. 3, 339–50, 4 figs. [30 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1960, v. 57, 478.]

BACTERIOPHAGES

MEYNELL, G. G. **Use of Superinfecting Phage for estimating the Division Rate of Lysogenic Bacteria in Infected Animals.** *J. General Microbiol.* 1959, Oct., v. 21, No. 2, 421–37, 7 figs. [17 refs.]

It is known that a phage particle superinfecting a lysogenic bacterium will, in some conditions, enter the cell but not multiply. When the cell divides the superinfecting particle is passed to 1 only of the 2 daughter cells. If, therefore, every cell in a culture contains 1 superinfecting phage particle, the proportion of cells carrying the superinfecting phage will halve at each generation. The author has used this principle to measure the rate of division of *Escherichia coli* in mice.

The system used, *E. coli* lysogenic for λb superinfected with λhc, was first tested *in vitro*. After induction with UV light, the superinfecting phage gave plaques on *E. coli* CR 63 as well as on C 600, while λb grew on C 600 only, so that the proportion of superinfected cells was given by the ratio of the number of plaques on CR 63 to the number on C 600. Experiments in the mouse were based on the assumptions that (1) the distribution of the superinfecting particle among the progeny would remain the same whatever the time between divisions, and (2) the presence of the superinfecting particle would not alter the behaviour of the bacteria *in vivo*. A measured number of cells carrying a known number of superinfecting particles was inoculated into mice intravenously and the mice killed at intervals afterwards. Viable organisms were found to be removed from the blood almost at once, about 1% later being recoverable from the spleen. The proportion of these carrying the superinfecting phage did not change in 30 hours, indicating that no bacterial division occurred in the spleen during this time. However, this proportion was greater than that in the inoculum, either because superinfection was unstable (as sometimes happened *in vitro*, depending apparently upon the state of the bacteria at the time of infection) or because the spleen removed superinfected bacteria preferentially. For this reason the number of generations passed through was not calculated. *Janice Taverne*

Dénes, G. & Polgár, L. **Effect of Nitroacridine 3663 on Synthesis of Deoxyribonucleic Acid and Multiplication of T_2 Phage.** [Correspondence.] *Nature.* 1960, Feb. 6, v. 185, 386, 1 fig.

Keck, K., Mahler, H. R. & Fraser, D. **Synthesis of Deoxycytidine-5'-Phosphate Deaminase in *Escherichia coli* Infected by T2 Bacteriophage.** *Arch. Biochemistry.* 1960, Jan., v. 86, No. 1, 85–8, 1 fig. [15 refs.]

Pietrzykowska, I. **Studies on the Mechanism of UV Induction of the Lysogenic Phage. I. Effect of Versene.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 12, 507–12, 4 figs.

Kjems, E. **Studies on Streptococcal Bacteriophages 3. Hyaluronidase produced by the Streptococcal Phage-Host Cell System.** *Acta Path. et Microb. Scandinavica.* 1958, v. 44, No. 4, 429–39, 3 figs. [16 refs.]

Lysogenic phages from Group A haemolytic streptococci form plaques surrounded by haloes on indicator strains which have hyaluronic acid capsules, and the phage lysates contain free hyaluronidase [Kjems, this *Bulletin*, 1958, v. 33, 797]. About one-third of the hyaluronidase activity of a lysate was deposited with the phage upon centrifugation, but about two-thirds of the activity was removed with the phage upon adsorption to sensitive bacteria. A third of the hyaluronidase activity of a lysate therefore appeared to be associated with phage fragments which did not sediment but which adsorbed to host cells. It seems likely that hyaluronidase is associated with the phage tail, and many free phage tails were seen in electron micrographs.

Phage antisera were found to inactivate hyaluronidase in the lysates. 7 different lysates were tested and serological differences were observed between the hyaluronidases they contained, as well as between phage hyaluronidase and hyaluronidase from streptococci. It was confirmed that the hyaluronidase produced depended upon the phage strain by showing that that present in a phage stock grown on one indicator strain differed serologically from that produced by another phage grown on the same strain. *Janice Taverne*

Gáspár, G. & Tolnai, G. **Studies on a *Cl. perfringens* Phage.** *Acta Microbiologica.* Budapest. 1959, 6, No. 4, 275–81, 3 figs.

A phage lysing *Clostridium welchii* [obtained from Guelin, this *Bulletin*, 1955, v. 30, 804] was titrated by counting plaques formed on bacteria growing in Wilson and Blair medium containing a reduced concentration of ferrous sulphate. A one-step growth curve was constructed for the phage, a neutralization test was done with antiserum prepared in rabbits, and the heat stability of the phage was investigated. In none of these properties did the phage differ significantly from aerobic phages. *Janice Taverne*

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

Deutschen Gesellschaft F. Hyg. U. Mikrobiol. Bericht über die 27. Tagung vom 22.–25. April 1959 in Essen. [**The German Society of Hygiene and Microbiology. Report on the 27th Session held on 22 25th April 1959, in Essen**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 176, Nos. 3/6, 161–411, numerous figs. [Numerous refs.]

The whole of this number of the journal is occupied by the proceedings of the German Society of Hygiene and Microbiology held in Essen in April 1959, and consists of 48 papers devoted to aerial hygiene, bacteriology and virology. The contributions are too numerous to abstract in detail, and only a selection of the more notable ones will be reviewed here. The topic of pollution of the air with smoke and sulphur dioxide and its effect on health is dealt with in a number of papers in which conditions in various parts of England and Germany are described. The papers in the section devoted to bacteriology are mostly prin

n the form of abstracts, and cover such subjects as hemoautotrophic bacteria, bacterial genetics, soil bacteriology, L colonies in *Proteus mirabilis* and the cology of yeasts. The section on virology comprises he greater part of the published matter, and opens vith a valuable and magnificently illustrated paper by D. PETERS on *The Morphology of Viruses Pathogenic for Animals and Man* (pp. 259–294). The morphology f poliomyelitis virus, the adenoviruses, herpes and myxoviruses as seen in electron microscope preparations s first reviewed, and the main part of the paper is then devoted to a description of the morphology of the pox viruses which is mostly based on the author's own work in this field. Vaccinia virus has been the object of greatest study, and a surprisingly complex morphology has been revealed by means of graded enzymatic hydrolysis and ultramicrotomy. It has also been possible to establish a tentative developmental cycle; virus material first appears after 6–8 hours as a zone of condensation in the cytoplasm, in which numerous oval membranes appear, gradually developing into mature elementary bodies. It has not been established with certainty whether the immature elementary bodies are infectious.

Problems of practical immunology are reviewed by G. HENNEBERG (*Virus Vaccines and Vaccinations*, pp. 301–321). The virus diseases of man and animals are summarized in tables, which provide information on the severity of the disease, its economic importance, the duration of immunity after infection, and whether a vaccine is available. In *Prevention and Control of Virus Influenza in Military Units* (pp. 327–331), G. FINGER discusses the control of influenza in the German army. During the pandemic of 1957–1958 about 44,000 cases occurred in the Bundeswehr among a total strength of 120,000 men; it was considered that vaccination would not be a practical measure and the epidemic was controlled by the isolation of the patients. 2 papers follow on the photometric haemagglutination test, originally developed by Drescher and described in a series of publications abstracted in this *Bulletin* [1959, v. 34, 1056; 1958, v. 33, 406 *bis*]. The effect of live and killed vaccines in creating immunity to Teschen disease in pigs is described by A. MAYR (pp. 341–345). The disease closely resembles human poliomyelitis, and the ease with which the virus can be made to multiply in cultures of pig kidney tissue has made it possible to produce a formalin-inactivated adsorbed vaccine. After 90 passages in tissue culture the pathogenicity of the virus had decreased, and a live vaccine has been developed with attenuated virus of a high passage level. It produced satisfactory levels of neutralizing antibody in young pigs when given orally or by subcutaneous injection, and also conferred protection against subsequent intracerebral challenge with virulent virus. In a paper by F. MÜLLER (*The Demonstration of Complement-Fixing Antibodies in Infectious Mononucleosis*, pp. 350–355) the development of a new diagnostic test for glandular fever is described. Lipids extracted from washed bovine red cells with 96% ethanol at room temperature are used as antigen in a complement-fixation test after suitable dilution in veronal buffer. In an examination of the sera of 16 patients with the clinical manifestations of infectious mononucleosis the complement-fixation test gave a positive result in a titre of 8 or higher in 14 instances, whereas only 8 positive results were obtained in the heteroagglutinin test. The Paul-Bunnell test is compared with the bovine red cell lysin test in a paper by K. MAI (*Advantages of a Bovine Red Cell Lysin Test in the Diagnosis of Infectious Mononucleosis*, pp. 367–370).

A paper by Gisela ENDERS-RUCKLE (*Enteroviruses as a Supposed Cause of the so-called Vesicle Disease*, pp. 389–400) is of particular interest. An outbreak of a disease characterised by a vesicular exanthem occurred in Marburg, Germany, in October and November 1958. Strains of virus were isolated in monkey kidney and human amnion cells from stools, throat washings and the contents of a vesicle. The strains could be divided into 4 groups on the basis of their behaviour in tissue culture, and 3 of the groups were also distinct serologically. In neutralization tests a relationship to ECHO viruses types 5 and 10 was observed in some strains, and the remainder could not be identified.

D. J. Bauer

WESSLÉN, T., ALBERTSSON, P. Å. & PHILIPSON, L. **Concentration of Animal Viruses using Two-Phase Systems of Aqueous Polymer Solutions.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 4, 510–20. [10 refs.]

Concentration and purification of vaccinia, mumps, Newcastle disease, influenza, ECHO and adenoviruses was attempted by means of partition in 2-phase polymer systems. In dextran-methylcellulose systems, no partition was obtained with ECHO 7 virus, whereas vaccinia, mumps, NDV and influenza were concentrated in the dextran phase. With dextran-polyethylene glycol systems all the viruses tested were concentrated in the dextran phase or in the interphase, giving recoveries of at least 99%. By the combined use of dextran-methylcellulose and dextran-polyethylene glycol systems, influenza and adenoviruses could be concentrated up to about 200 times. *H. G. Pereira*

BREESE, S. S., Jr. & TRAUTMAN, R. **Examination of Spray-Droplet Particle Counting as a Measure of Virus Concentration.** *Virology.* New York. 1960, Jan., v. 10, No. 1, 57–72, 6 figs. [12 refs.]

"Model systems using known mixtures of polystyrene latex solutions have been used to study the spray-droplet method for determining particle concentration. Neither the binomial nor the Poisson distributions are applicable to the counts of particles in individual droplet residues. Both distributions are useful, however, for mathematical deductions about counting errors in the totality of data. The chi-square test for the homogeneity of a series of droplets is verified. The relationship of the critical region to the value of the ratio of the numbers of particles present is demonstrated, and the reasons for selecting the 5% level are given. A chart is presented from which, in the case of determining the concentration of an unknown particle such

as a virus, the level of error to be expected may be determined. This level is in terms of the total number of particles counted and the ratio of the numbers of known to unknown particles."

ISAACS, A. **Metabolic Effects of Interferon on Chick Fibroblasts.** [Correspondence.] *Virology.* New York. 1960, Jan., v. 10, No. 1, 144–6, 1 fig.

Trypsin-dispersed suspensions of chick embryo cells incubated overnight with interferon and then trypsinized, thoroughly washed and reincubated showed significantly increased glycolysis as compared with control untreated cells. This was revealed by a striking increase in CO_2 evolution (2 to 3 times higher than controls) and a less marked stimulation of oxygen uptake (30 to 50% higher than controls). Evidence is presented to show that this effect is specifically caused by interferon. The possible relationship between metabolic changes and viral interference is discussed.

H. G. Pereira

BERNKOPF, H., NISHMI, M. & ROSIN, A. **Effect of Active and Inactive Vaccinia Virus Preparations on Human Amnion Cell Cultures.** *J. Immunology.* 1959, Dec., v. 83, No. 6, 635–9, 5 figs. [10 refs.]

In previous work [this *Bulletin*, 1959, v. 34, 584] the authors showed a toxic action of vaccinia virus on human white blood cells and cultures of mouse macrophages. They now demonstrate 2 different types of reaction in human amnion cell cultures exposed to heavy concentrations of either infectious or ultraviolet-irradiated vaccinia virus. With infectious virus, rounding of cells and loss of adhesion to glass began to be noted after 6–8 hours. In stained preparations both nucleus and cytoplasm were eosinophilic. Inoculation of monolayer cultures with diluted virus suspensions was followed by focal formation of countable plaques. After inoculation of cultures with irradiated virus, however, the picture was quite different. Between 12 and 24 hours the polygonal cell lengthened and curious whorled formations of cells occurred in previously uniform layers. The cells retained their normal staining characteristics. Within 2–4 days the cell sheet had completely disappeared, to be replaced by a net-like system of cells looking very like conventional tissue culture "fibrocytes".

The changes produced by both active and inactivated virus were prevented by antivaccinial serum. Centrifugation experiments indicated that the toxic properties were associated with the virus particles. The experiments were performed with 4 different strains of vaccinia virus.

Colin Kaplan

SALZMAN, N. P. **The Rate of Formation of Vaccinia Deoxyribonucleic Acid and Vaccinia Virus.** [Correspondence.] *Virology.* New York. 1960, Jan., v. 10, No. 1, 150–52, 1 fig.

BROWN, A., MAYYASI, S. A. & OFFICER, J. E. **T Agglutination of L Cells by Vaccinia Virus. I The Cell Virus Interaction related to the A glutination Reaction.** *J. Immunology.* 19 Nov., v. 83, No. 5, 521–8, 4 figs. [10 refs.]

Having previously shown that the agglutination L cells by vaccinia virus could be used as the ba for a titration method [this *Bulletin*, 1960, v. 35, 40 the authors went on to investigate other aspects of t cell virus relationship. Compared with chick cel HeLa cells and human liver cells, L cells were resista to both virus multiplication and release. Agglutinati was observed 2 hours after infection, but unequivo evidence of virus multiplication was not obtained befo 10 hours. Cells killed by a variety of agents could n be agglutinated even by large doses of virus. Expe ment with inhibitors of glycolysis indicated that agg tination was associated with a functioning glycoly mechanism but was independent of the pathwa inhibited by azide or amethopterin. Cell agglutinati was not inhibited or only slightly inhibited by previc ultraviolet irradiation of the virus. Time lap cinematography suggested that agglutinated cells wo held together by some cohesive force or substan possibly the same as that responsible for the adheren of normal cells to glass. Agglutinated cells were read dispersed by trypsin or papain. When re-inoculat into flasks, such cells partially re-agglutinated. T ability to undergo re-agglutination was lost after 3 day this was at about the same time that agglutinated ce started to die. The mechanism of agglutination was r related to that of influenza haemagglutination.

Colin Kaplan

GIL FERNÁNDEZ, Carmen. **Persistence of Herp Simplex Virus in HeLa Cells.** [Correspondenc *Nature.* 1960, Jan. 23, v. 185, 268.

When isolated HeLa cells which had survived t cytopathic effect of herpes simplex virus were cultur in a medium containing herpes antiserum, colonies morphologically normal cells formed. About 1 in 1 of these cells gave rise to a microplaque, and t ability to carry virus persisted through 29 subcultur In the absence of antiserum the localized cytopat changes became confluent. Sub-lines which did n give rise to plaques could also be derived from survivi cells. They were still sensitive to virus, however, b 10–100 times more virus than usual was required produce a cytopathic effect.

It is suggested that the virus may persist in the cultures because the lesser sensitivity of the ce reduces its rate of spread. (Herpes is known to be a to pass directly from cell to contiguous cell wh cultured in the presence of antiserum [this *Bulle* 1955, v. 30, 823; 1957, v. 32, 811].) *Janice Taverne*

OVERMAN, J. R. & LEWIS, A. M., Jr. **Effects of Hi Pressures on Influenza Viruses.** *Proc. Soc. Exp Biol. & Med.* 1959, Nov., v. 102, No. 2, 329– 2 figs.

The effect of high pressures at temperatures bel freezing point on various biological properties

influenza virus types A, B and C was investigated. The sensitivity of haemagglutinins to high pressures varied considerably even among closely related virus strains. Virus infectivity and antigenicity were more sensitive to high pressures than haemagglutinating activity.

The results suggest that virus inactivation by high pressures is not a suitable procedure for the preparation of vaccines. *H. G. Pereira*

White, D. O. **The Mechanism of Natural Resistance of the Allantois to Influenza Infection.** *Virology.* New York. 1959, Dec., v. 9, No. 4, 680–90, 2 figs. [12 refs.]

Variation of the resistance of chick embryo chorio-allantoic membranes to infection by influenza virus was studied by measuring the susceptibility to infection and virus yield on suspended pieces of chorio-allantoic membranes [this *Bulletin*, 1958, v. 33, 710] from eggs of varying ages.

Virus yields were found to be unrelated to susceptibility of membranes to infection by small virus doses, suggesting that increased resistance to infection is due not to a reduction in the number of cells able to support virus multiplication, but to a lower probability of infection of individual cells. Changes in resistance to infection could not be explained by variations in virus adsorption, penetration or liberation.

Experiments designed to demonstrate inheritable variations in infectivity of individual virus particles gave negative results. *H. G. Pereira*

White, D. O. **Some Aspects of Influenza Virus Multiplication in the Surviving Allantois-on-Shell System.** *Virology.* New York. 1960, Jan., v. 10, No. 1, 21–8, 3 figs. [10 refs.]

A study of the adsorption of influenza A virus to surviving bits of chick chorio-allantoic membranes showed that an average allantoic cell is able to adsorb about 1,000 virus particles.

Virus liberation from membranes inoculated with small virus doses could first be detected after 7 to 9 hours' incubation but could be delayed for several hours. Taking 7 to 9 hours as time 0 the average delay in virus liberation was of 2 to 4 hours, this value being constant for membranes from eggs of different ages.

The growth rate of influenza virus was constant on membranes of varying susceptibilities and it is suggested that this may be due either to higher susceptibility of cells on the deeper layer of the allantoic onto which first cycle virus progeny is able to spread [this *Bulletin*, 1959, v. 34, 829], or to decrease in virus infectivity occurring some time after liberation. *H. G. Pereira*

Gamba, F. & Gasparini, V. Ricerche comparative sul comportamento del virus influenzale nei riguardi delle emazie di pollo fresche e formolate. [**Comparative Studies on the Behaviour of Influenza Virus in Relation to Fresh and Formalinized Chicken Red Cells**] *Riv. Istituto Sieroterap. Ital.* 1959, Nov.–Dec., v. 34, No. 6, 419–26, 4 figs. on 2 pls.

The English summary appended to the paper is as follows:—

"Investigations were carried out on formalin treated chicken red cells, which were compared to untreated red cells by influenza virus adsorption and elution tests and by electron microscopy.

"It has been observed that even after 3 month's storage at + 4°C, formalinized cells can be practically used in hemagglutination test, although their adsorptive capacity toward influenza virus is slightly impaired. Therefore, the use of formalinized red cells in routine influenza serology is suggested."

Noll, H. & Youngner, J. S. **Virus-Lipid Interactions. II. The Mechanism of Adsorption of Lipophilic Viruses to Water-Insoluble Polar Lipids.** *Virology.* New York. 1959, July, v. 8, No. 3, 319–43, 3 figs. [28 refs.]

In an extension of previous work [this *Bulletin*, 1959, v. 34, 687] on the adsorption of viruses on to cholesterol the authors have investigated the adsorptive powers of a number of compounds containing carboxyl, hydroxyl, amino or carbamyl groups. Adsorption was carried out by passing the PR8 strain of influenza virus through a column or by grinding it with the compound in a mortar. Fatty acids, alcohols, amines and an amide containing a chain of 13–21 carbon atoms adsorbed 80–100% of the virus. Type B strains (Lee, Allen, MB) were strongly adsorbed by hexadecylamine but were less well adsorbed by cholesterol and palmitic acid. In saturation experiments it was found that palmitic acid had an adsorption capacity of 55,000 haemagglutinating units per gm., and hexadecylamine of more than 200,000 units, compared with 15,000 units for cholesterol. The virus present in 50 cc. of fluid could be removed almost completely by shaking with 10 mgm. of hexadecylamine, and a 50–100-fold concentration of the virus could easily be achieved by this method. Virus adsorbed on to hexadecylamine retained only 0·003% or less of its initial infectivity, but was highly antigenic when injected into guineapigs, which responded with inhibition titres higher and more persistent than those obtained with aqueous vaccines. In experiments with other viruses it was found that lipids would also adsorb Newcastle disease, herpes, vaccinia, infectious canine hepatitis and B viruses, whereas poliomyelitis, Coxsackie and ECHO viruses were not adsorbed at all; lipophilic and hydrophilic groups of viruses can therefore be distinguished. *D. J. Bauer*

Reimold, Gertrud. Über die Wechselwirkung von Seruminhibitoren, Hühnererythrozyten und Influenzaviren. [**The Interaction of Serum Inhibitors, Fowl Erythrocytes and Influenza Viruses**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Aug., v. 118, No. 2, 121–34. [11 refs.]

In a comparison of the haemagglutination-inhibition titres of 8 human sera against the FM 1 and Lee strains of influenza virus it was found that the red cells of one chicken gave consistently lower titres than those of another. The same difference was still observed after the sera had been treated with trypsin in order

to remove unspecific inhibitor. A rise in inhibition titre of up to 32-fold was observed when the time of contact of serum and virus was prolonged to 4 hours before adding the red cells, and a similar effect could still be observed after the sera had been treated with trypsin. *D. J. Bauer*

FURESZ, J. **Studies on Inhibitors of Influenza Virus Haemagglutination in Normal Rabbit and Ferret Sera.** *Canadian J. Microbiol.* Ottawa. 1959, Oct., v. 5, No. 5, 505–11. [18 refs.]

Non-specific inhibitors of influenza virus haemagglutination were removed from normal rabbit and ferret sera by absorption with purified preparations of influenza A-prime and B strains. The thermolabile Chu inhibitor was absorbed by A-prime but not by B strains whereas the thermostable Francis inhibitor was absorbed only by the B strain. Heat inactivation or periodate treatment of the viruses did not abolish their capacity to combine with inhibitors. *H. G. Pereira*

SETO, J. T., HICKEY, Betty J. & RASMUSSEN, A. F., Jr. **Sialidase Activity and Related Properties of Influenza A2 Viruses.** *Virology.* New York. 1959. Dec., v. 9, No. 4, 598–611, 3 figs. [25 refs.]

Sialidase activity of 5 strains of Asian influenza (A2) virus and of A (PR8, Swine, NWS), A-prime (FM1, Perez/57), B (Lee) and Newcastle disease virus was measured by a method based on the estimation of residual non-dialysable sialic acid in virus-substrate (urine mucoprotein) mixtures incubated at 37°C. for 20–24 hours.

Sialidase activity of A2 strains was greater than that of other virus strains even though the latter often had higher haemagglutinin titres. There was no strict correlation between sialidase activity and virus elution from red cells or sensitivity to heat-resistant haemagglutination inhibitors of human serum, horse serum and urine mucoprotein. Sialidase activity of A2 strains was more heat stable than their haemagglutinins; of the other viruses included in this study, only the Swine strain behaved similarly to A2 in this respect. Evidence is presented suggesting that viral toxicity may be dependent of sialidase activity. *H. G. Pereira*

HOLPER, J. C. & MARQUIS, G. S., Jr. **Inhibition of Influenza Virus Multiplication in Swine Kidney Cells by Lactalbumin Hydrolysate.** *J. Infect. Dis.* 1959, Nov.–Dec., v. 105, No. 3, 288–92.

Multiplication and cytopathic effect of an influenza A-prime virus strain in cultures of swine kidney cells were inhibited by lactalbumin enzymatic hydrolysate concentrations of 1% or higher added to the culture medium. This effect of lactalbumin hydrolysate was not due to a direct action on the virus or to inhibition of virus adsorption but appeared to affect some process occurring during the virus multiplication cycle. No inhibition was detected with media containing dextrose, NaCl, amino acids and proteins in concentratio corresponding to a 1·5% dilution of lactalbum hydrolysate. *H. G. Pereira*

GOSTLING, J. V. T. **Influenza *A'* Infection of Culture Cells of Whole Mouse Embryos.** [Correspo dence.] *Nature.* 1960, Jan. 30, v. 185, 328.

EATON, M. D., JEWELL, Marjorie & SCALA, A. **Formation of Noninfectious Viral Hemaggl tinins in Ascites Tumor Cells.** *Virology.* Ne York. 1960, Jan., v. 10, No. 1, 112–26. [15 refs.

Mouse ascites tumour cells (Ehrlich and Krebs inoculated *in vitro* with influenza A (PR8) or Newcast disease virus were partially or totally damaged as show by cell lysis, permeability to eosin and reduction respiration rate and tumour producing capacity. T degree of cell damage was related to size of vir inoculum. This effect was accompanied by production non-infectious haemagglutinin which reached higher titr in Krebs 2 than in Ehrlich's ascites cells. Haema glutinin production by Krebs 2 cells was greatly reduce when glucose was used instead of lactate as substrat The same did not occur with Ehrlich's cells. With t glucose medium, anaerobic conditions favoured haema glutinin production by Krebs 2 and had little or n effect on the behaviour of Ehrlich's cells. Virus pr duction by chorioallantoic membranes was favoured b aeration.

Production of haemagglutinin by ascites cells developing tumours inoculated *in vivo* with PR8 vir is also reported. *H. G. Pereira*

DEICHMAN, G. I., GRIGOR'EVA, A. G. & VENUSTO N. V. **The Effect of the Concentration of Liv Virus in Influenza Vaccine upon its Antigen Activity.** *Problems of Virology.* London. 195 v. 3, Nos. 5/6, 385–90. [Translated from Russian

Live strains of influenza A-prime, B and C we tested for immunizing power in groups of 12 to volunteers receiving varying virus doses by the intr nasal route. Antibody rises following vaccination we measured by haemagglutination-inhibition and efficac of immunization was tested by challenge with virule homologous virus. 3 groups of volunteers receivi vaccine doses with infective titres of 10^6, 10^7 and 10^8 respectively showed clinical reactions with frequenci directly related to vaccine dose. A direct relationshi was also observed between vaccine dose and frequenc of virus recovery from nose and throat, rise in antibod titre and resistance to subsequent infection.

Influenza B vaccine with infectivity titres of 10^6 an 10^8 gave rise to clinical reactions in all but 1 of 2 volunteers with virus recovery from 15 of 16 volunteer given the larger virus dose and from 6 of 12 volunteer in the lower dose group. Protection against secondar challenge was observed in 12 volunteers tested in eac group. As in the case of A-prime strain, antibod responses were related to vaccine dose.

Influenza C vaccines with infectivity titres of 10^6 an

10^8 caused mild and infrequent clinical reactions, and there was a direct relationship between the dose of vaccine and the frequency of virus recovery and the rise in antibody titre. *H. G. Pereira*

WOODHOUR, A. F., JENSEN, K. E. & WARREN, J. **Antibody Response to Influenza Vaccines combined with Hexadecylamine.** *Proc. Soc. Exper. Biol. & Med.* 1960, Jan., v. 103, No. 1, 200–204, 5 figs.

"Hexadecylamine in levels up to ·5 mg/ml is well tolerated by man and animals. A single injection into guinea pigs of influenza vaccines containing this material results in rapid production of antibody levels which exceed those elicited by control vaccines. Preliminary results in man suggest that adjuvants of this nature may be most efficacious in a population receiving primary influenza experience."

GINZBURG, Y. & TRAUB, A. **A Spectrophotometric Method for the Determination of Hemadsorption: its Use for the Study of Viral Nutritional Requirements.** *Virology.* New York. 1959, Dec., v. 9, No. 4, 671–9, 5 figs.

"A quantitative spectrophotometric method for the determination of the production of Newcastle disease virus (NDV) by mammalian cells grown *in vitro* is described. The method is based on the ability of infected cells to adsorb chicken red blood cells (RBC). The hemoglobin of the adsorbed RBC is assayed spectrophotometrically. Between the seventh and eleventh hour post infection (p.i.) a linear relationship was found to exist between the extent of RBC adsorption and the percentage of intracellular virus yield. The method has been used for the nutritional evaluation of glutamine and various carbohydrates."

KLEIN, M., EARLEY, Elizabeth & ZELLAT, J. **Isolation from Cattle of a Virus related to Human Adenovirus.** *Proc. Soc. Exper. Biol. & Med.* 1959, Oct., v. 102, No. 1, 1–4, 1 fig.

Inoculation of foecal swab material from an apparently normal cow into cultures of calf kidney cells gave rise to cytopathic effect resembling that of adenovirus types 3, 4 and 7. The agent responsible for this effect could be propagated in cultures of calf kidney cells reaching titres of 10^{-2} to 10^{-3} per 0·1 ml of tissue culture fluid. No activity could be detected in HeLa cell cultures, adult or suckling mice, chick embryos, guineapigs, rabbits or hamsters. It could not be detected by haemagglutination or haemadsorption tests with guineapig, sheep, cow, chicken or human red cells. It was not neutralized by antisera to ECHO viruses types 1–19; Coxsackie B viruses types 1–5; polio virus types 1–3; herpes simplex; B virus; measles; mumps; influenza A, B, swine, Asian; haemadsorption viruses types 1 and 2 or adenoviruses types 1–7. Sera from guineapigs and hamsters immunized against the bovine strain reacted by complement fixation with human adenovirus antigens.

A possible relationship of the bovine agent to an as yet unidentified human adenovirus was suggested by the finding that it was neutralized by human gamma globulin and by a high proportion of human adult sera but not by sera from infants. *H. G. Pereira*

KLEMPERER, H. G. & PEREIRA, H. G. **Study of Adenovirus Antigens fractionated by Chromatography on DEAE-Cellulose.** *Virology.* New York. 1959, Dec., v. 9, No. 4, 536–45, 5 figs. [15 refs.]

PEREIRA *et al.* [this *Bulletin*, 1959, v. 34, 831] have previously described 3 antigens A, B and C separated from adenovirus by immune immunoelectrophoresis. Antigen A represents adenovirus group antigen and C the type specific antigen. Antigen B is the protein fraction responsible for the early cytopathic change [*ibid.*, 1959, v. 34, 502] and probably cell detachment observed with concentrated adenovirus inoculum [*ibid.*, 1959, v. 34, 293]. Now adenoviruses, types 2 and 5, have been fractionated by adsorption on to DEAE-cellulose columns and elution with increasingly strong solutions of sodium chloride. It was found that the antigens were adsorbed from 0·01 M sodium phosphate solution onto the column. At 0·05 M NaCl antigen C (intact type specific virus) was eluted, at 0·2 M the protein antigen B causing early cytopathic effects and at 0·3 M NaCl the group specific A antigen. Antigens A and C were quite distinct serologically, but B and C showed some tendency for fusion of their precipitin lines suggesting partial antigenic identity.

A. J. Beale

COLOBERT, L. & FONTANGES, R. Titrage de l'activité hémagglutinante et da l'activité enzymatique de *Myxovirus parainfluenzae I* (virus *Sendai*). [**The Haemagglutinating and Enzymatic Activities of Sendai Virus**] *C.R. Soc. Biol.* 1959, v. 153, Nos. 8/9, 1382–6, 3 figs. [Refs. in footnotes.]

The haemagglutinating activity of Sendai virus (*Myxovirus parainfluenzae* 1) was estimated by measuring the sedimentation rate of virus red cell suspensions. Formalin-treated cells had to be used to avoid haemolysis. Sendai haemagglutinin prepared by ether extraction had no effect on red cell sedimentation rate but could be detected by the pattern of the cell deposit (shield formation). It is suggested that this effect may be due to a lowering of electric charge causing the red cells to adhere to glass [this *Bulletin*, 1959, v. 34, 291].

The kinetics of the haemolytic activity of Sendai virus was studied by measuring at varying times the optical density of supernatants of virus-cell suspensions incubated at 37°C. The process followed an exponential curve but the reaction constant varied considerably when different batches of red cells were used.

H. G. Pereira

ZHDANOV, V. & BUKRINSKAYA, A. **Further Considerations on Nomenclature of Parainfluenza Viruses.** [Correspondence.] *Virology.* New York. 1960, Jan., v. 10, No. 1, 146–9.

Haemadsorption virus types 1 and 2, Sendai, mumps and Newcastle disease viruses were compared by serum

neutralization, haemagglutination-inhibition and complement-fixation tests. With rabbit antisera no cross reactions were detected by serum neutralization whereas by haemagglutination inhibition, haemadsorption 1 sera cross-reacted with haemadsorption 2 antigen and Newcastle disease serum with Sendai antigen. Complement-fixation tests revealed common antigens in Sendai, mumps and Newcastle disease virus.

Apart from antigenic structure, haemadsorption 2 and Sendai viruses differ from each other in cytopathology, growth in embryonated eggs and human pathogenicity and the authors suggest that these 2 agents should be considered as separate para-influenza viruses. [See also ANDREWES *et al.*, this *Bulletin*, 1959, v. 34, 1056.]

H. G. Pereira

PELON, W. & MOGABGAB, W. J. **Further Studies on 2060 Virus.** *Proc. Soc. Exper. Biol. & Med.* 1959, Nov., v. 102, No. 2, 392–5, 1 fig.

Inoculation of 2060 virus [this *Bulletin*, 1957, v. 32, 629] into monkey kidney cultures gave rise to a typical cytopathic effect which was correlated in time and intensity with the amount of infective virus present in culture fluids. Omission of vitamins or glutamine from the synthetic medium (EAGLE, *J. Exper. Med.*, 1955, v. 102, 37) used for virus propagation resulted in reduced virus yields. Both virus yield and sensitivity of cultures to infection were 10 to 100 times higher in cultures maintained at *p*H 7·0–7·2 than at *p*H 7·6–7·8. A comparison of 2060 and JH [this *Bulletin*, 1959, v. 34, 1191] viruses by serum neutralization with monkey and rabbit antisera or human convalescent sera revealed antigenic relationship but non-identity of the 2 viruses. Neutralizing antibody rises for both viruses were detected in 32 of 57 human serum pairs whereas the remaining pairs gave rises for only one of the 2 viruses. Antibody rises were detected in 16 of 44 patients with mild afebrile respiratory illness with coryza as the predominant symptom. *H. G. Pereira*

SABIN, A. B. **Reoviruses. A New Group of Respiratory and Enteric Viruses formerly classified as ECHO Type 10 is described.** *Science.* 1959, Nov. 20, v. 130, 1387–9, 1 fig. [23 refs.]

ECHO type 10 virus has long been recognized as "odd man out" in the enterovirus family. Now Sabin, as a result of a study of 11 strains of ECHO 10 virus, has suggested that they be removed from the enterovirus family (this proposal has the approval of the Committee on Enteroviruses set up by the National Foundation) and grouped together to form the reoviruses. This name is meant to stress the predilection of these viruses for both the respiratory and enteric tracts.

The viruses have been isolated from the stools of healthy children, from children with diarrhoea, from several outbreaks of minor illness in an orphanage in Washington, D.C., from an outbreak of rhinitis in chimpanzees and from cattle. The virus has also been isolated from monkeys. Antibodies have been found rabbits and guineapigs as well as the species fr which the virus has been isolated. The properties this group of viruses have been studied by using strains of the virus. They are ether resistant a approximately 72 mμ in size. Monkey kidney cells a the preferred method for isolation and in these ce they produce distinctive cytopathic effects consisting granular degenerate cells with more or less int nuclei. In the cytoplasm inclusions of varying size a shape occur. These are eosinophilic and stain bl with Giemsa. The prototype "Lang" strain also pr duces cytopathic effects in guineapig, swine, cat and d kidney cells and partial effects in kidney cells fr calves and rabbits.

Reoviruses multiply in newborn mice and some the strains produce clinical signs of disease with lesio in the nerve cells, myocardium and liver but lesio are rare in the brown fat or in the pancreas and not resemble those due to Coxsackie A or B virus Adult mice remain well. The prototype strain mul plies in chick embryos and following intracereb inoculation into monkeys occasional animals die wi lesions in the ependymal lining of the ventricles and the choroid plexus. One strain was isolated from chi panzees with rhinitis and this strain causes a comm cold syndrome following nasal installation into chi panzees. Reoviruses cause haemagglutination of huma group O red cells. The red cell receptors are n affected by RDE but are destroyed by potassium peri date. All the strains share a common complement-fixi antigen but can be divided into 3 distinct serologic groups by means of neutralization or haemagglutinati inhibition tests.

The first serological type of reovirus has as its prot type the "Lang" strain and includes a strain isola from normal children in Mexico, the simian vi SV 12 and strains isolated by Dr. L. ROSEN a his colleagues in Bethesda from an orphanage Washington, D.C. The prototype strain for type 2 the D 5 strain isolated from a child with diarrho [RAMOS-ALVAREZ and SABIN, this *Bulletin*, 1958, v. 3 1115] and includes the strains derived from an epidem of rhinitis in chimpanzees, a simian virus strain SV 5 a strain "Amy" recovered from a child with steato rheic enteritis (Sabin, *Ann. N.Y. Acad. Sci.*, 1956, v. 6 226), strains isolated from a healthy child in Mexi and 2 strains from the Washington orphanage. T prototype of the type 3 strains is "Dearing" deriv from a child with diarrhoea [Ramos-Alvarez and Sabi this *Bulletin*, 1958, v. 33, 1115]. Rosen and his co leagues also recognized type 3 reovirus and selecte a strain "Abney" as the prototype. This strain w a representative of 12 strains recovered from childr in the Washington orphanage and appears identical wi the "Dearing" strain and other type 3 strains studi in Sabin's laboratory. Rosen and F. R. ABINANTI ha recovered 4 type 3 strains from naturally infect cattle.

The exact pathogenic propensities of this new gro of viruses for man have yet to be fully worked ou but their profound effects on suckling mice sugges they may have similar effects in new-born human being

A. J. Beale

HSIUNG, G. D. **Use of Human Kidney Cultures in the Study of Enteroviruses.** *Proc. Soc. Exper. Biol. & Med.* 1959, Dec., v. 102, No. 3, 612–16, 6 figs.

Human kidney cultures from babies or adults obtained at operation or necropsy were grown successfully after trypsinization, in medium containing 20% calf serum. Babies under 2 years yielded better cultures than adults. 37 out of 44 attempts were successful when obtained up to 24 hours after death. All kidneys removed at operation grew well and 4 out of 6 removed within 6 hours of death, but only 2 out of 17 removed 0–24 hours after death. Baby human kidney cultures were at least as sensitive to infection with a wide range of enteroviruses as rhesus monkey kidney cells (polio 1, 2, 3, Coxsackie A9, B1–5 and ECHO 1–14). Indeed for ECHO 11 virus the human kidney cells appeared superior, thus virus was recovered from 8 out of 19 faecal specimens in these cells against 3 out of 19 in rhesus monkey kidney cells. Adult human kidney cells were also excellent for polioviruses and ECHO 7 and 10 but not as sensitive or showing as complete cellular degeneration to the other ECHO viruses. The potential value in diagnostic virology of human kidney cells obtained from necropsies on children is stressed. These cells have been maintained in medium containing 2% calf serum for 2 months, and no latent viruses have been detected. The reason for the different susceptibility of kidney cells from babies and adults is unknown.

A. J. Beale

GODTFREDSEN, Annelise & VON MAGNUS, H. **Routine Diagnosis of Enteroviruses using Tissue Culture Techniques. Experiences in Denmark during 1956–1958.** *Danish Med. Bull.* 1959, Nov., v. 6, No. 8, 264–9. [10 refs.]

The authors describe the results of examination of faecal samples sent in on a routine diagnostic basis from cases of suspected poliomyelitis or viral meningitis. 10% faecal suspension was added to 3–5 cultures of monkey kidney cells containing medium 199. As a precaution against cross contamination 3 control tubes were left after each series of infected tubes from 1 specimen. After 3 hours at 37°C. on a roller drum the inoculum was removed and the cultures nourished with bovine amniotic fluid. Cultures were kept for 14 days.

With this technique, which was found to be at least as sensitive as other methods and less prone to trouble from toxic faecal extract, polioviruses were isolated from 78 of 108 cases of paralytic poliomyelitis (44 type 1, 2 type 2 and 32 type 3). 264 virus isolations were made from 1,344 cases of suspected viral meningitis, 27 were poliovirus, 152 ECHO 9 viruses, 51 are as yet unidentified and all the others except 5 adenoviruses were members of the enterovirus group. The ECHO 9 strains were slightly different antigenically from the prototype Hill strain, but differed from other "prime" strains recently isolated from patients in that antisera to them gave considerably higher titres against them than against Hill. Also the strains were usually pathogenic for suckling mice on passage in tissue culture and 3 strains were pathogenic on direct isolation from stools [see EGGERS & SABIN, this *Bulletin*, 1960, v. 35, 406, for an analysis of the pathogenicity of ECHO 9 virus for suckling mice.] In a localized outbreak of meningitis 10 ECHO 9 isolations were made from 12 patients, but for the stools collected from random cases of meningitis the virus isolation was just under 20%, suggesting that the aetiology of many of these remains to be determined.

A. J. Beale

GREEN, R. H. & OPTON, E. M. **Photosensitization of Tissue Culture Cells and its Effect on Viral Plaque Formation.** *Proc. Soc. Exper. Biol. & Med.* 1959, Nov., v. 102, No. 2, 519–21, 2 figs.

If cell cultures overlaid with nutrient medium in agar containing neutral red are exposed to light the cell sheet degenerates. This occurs quite quickly, 2–3 hours being sufficient to destroy the cells. When the cells are infected with poliovirus the plaques are smaller and less numerous if cultures containing neutral red are exposed to light—noticeable changes occur with 15 minutes' exposure and severe changes after 45 minutes. Both fluorescent and incandescent light cause the changes. Degeneration was observed in monkey kidney, Hep 2 chick embryo and dog kidney cultures exposed to light and neutral red.

[The same basic observation has been reported by KLEIN and GOODGAL, *Science*, 1959, v. 130, 629.]

A. J. Beale

BOEYÉ, A. **Induction of a Mutation in Poliovirus by Nitrous Acid.** *Virology*. New York. 1959, Dec., v. 9, No. 4, 691–700, 3 figs.

Type 1 poliovirus and the RNA derived therefrom is inactivated by nitrous acid. The curve of inactivation for RNA is exponential, but for intact virus proceeds at a decreasing rate with increasing degree of inactivation. During inactivation of *d*-type virus or the RNA from it (*i.e.* virus giving a higher titre in the presence of high levels of bicarbonate), there was an increase in the proportion of $d+$ particles among the survivors. No evidence could be obtained that $d+$ particles were selected by nitrous acid, since enriching the d culture with $d+$ particles did not cause a proportionate increase in $d+$ survivors. It was therefore concluded that $d+$ mutants were induced by the nitrous acid. It was found that for assaying the poliovirus RNA (from a type 1 Brunhilde strain) a particular HeLa cell line Am-39 was the most sensitive of 3 HeLa cell lines tested.

A. J. Beale

WENNER, H. A. & DUBES, G. R., with the assistance of Margaret LENAHAN, P. KAMITSUKA & Margaret CHAPIN. **The Virulence and Immunogenicity of 23 C-Adapted Polioviruses. I. In Cynomolgus Monkeys following Inoculation by Alimentary and Intramuscular Routes.** *Amer. J. Hyg.* 1959, Nov., v. 70, No. 3, 335–50, 1 fig. [25 refs.]

The authors have previously described the selection of mutants of all 3 strains of poliovirus adapted to

grow first at 30°C. and finally at 23°C. [DUBES and CHAPIN, this *Bulletin*, 1957, v. 32, 292, and DUBES and WENNER, *ibid.*, 1958, v. 33, 533]. The strains adapted to grow at 23°C. grow poorly if at all on monkey cells maintained at 37°C. They are of greatly reduced virulence for monkeys, thus the type 1 Akron strain gave lesions in 2 out of 35 animals, the Brooks type 2 strain in 6 out of 35 and the Mabie type 3 strain 1 out of 31 animals inoculated intraspinally. It was found that after alimentary administration of virus to cynomolgus monkeys none of the animals became infected, nor did they show an immune response judged by the production of neutralizing antibodies or challenge with virulent virus. When the cold-adapted viruses were given by intramuscular inoculation again no sign of illness occurred but most of the animals responded with low levels of neutralizing antibodies and by a resistance to challenge with virulent virus. The response was best for the Brooks type 2 strain, all the animals responding to a dose of 10^6 plaque-forming units (RFU) per ml., whereas for the Akron type 1 and the Mabie type 3 strains at the same dosage 2 and 3 out of 10 failed to produce homotypic antibodies respectively.

The addition of a mineral oil adjuvant greatly enhanced the response to an intramuscular dose of the Akron strain of poliovirus. Thus, with a dose of 10^5 PFU per ml. none of 4 responded, at 10^6, 7 out of 9 and at 10^7, 3 of 3 responded with the production of type 1 antibodies. When adjuvant was omitted even a dosage of 10^7 PFU per ml. did not give rise to either antibodies or resistance to challenge. It appears, therefore, that the cold-adapted mutants although avirulent for monkeys have been so attenuated as to be incapable of significant multiplication or of providing any greater antigenic stimulus than would be due to the equivalent amount of dead poliovirus. *A. J. Beale*

HO, M. & ENDERS, J. F. **Further Studies on an Inhibitor of Viral Activity appearing in Infected Cell Cultures and its Role in Chronic Viral Infections.** *Virology*. New York. 1959, Nov., v. 9, No. 3, 446–77; 7 figs. [14 refs.]

The authors [this *Bulletin*, 1960, v. 35, 315] have previously shown that human kidney cells infected with the chick-embryo-adapted strain of type 2 MEF 1 poliovirus called RMC [ROCA-GARCIA *et al.*, *ibid.*, 1953, v. 28, 481] produce a viral inhibitory fluid (VIF) which inhibits the cytopathic effect and multiplication of all 3 types of poliovirus and also certain unrelated viruses. They showed that this VIF does not depend upon the presence of infective RMC virus for its action because VIF was not neutralizable by type 2 poliovirus antiserum and was still effective after the infectious virus had been removed by ultracentrifugation. Also the simultaneous inoculation of RMC virus and type 3 poliovirus did not give rise to an inhibitory effect.

More extensive studies are now reported. They show that VIF is produced in highest amounts 3–4 days after the addition of RMC virus and with 1 fluid change. VIF was produced not only in human kidney cells but also in human amnion cells and in HeLa cells. VIF was not produced by type 2 poliovirus inactivated by heat or by ultra-violet rays. VIF was not dialyable, it was relatively heat resistant, some activity bei retained after heating for 60 minutes at 56°C. withstood freezing and thawing. It appeared to be protein, being destroyed by trypsin, but was unaffect by ribonuclease. VIF inhibited the cytopathic effect vaccinia, ECHO 9 and Sindbis viruses and very slight the effect of herpes simplex. The effect of VI appeared to be about the same whether given befo or up to 3 hours after the inoculation of challen virus but was definitely less when added 7 or 16 hou after the addition of virus. The action of VIF w considerably greater if it was continuously present the medium, thus on changing the fluid, if VIF w omitted the effects still existed but were less pr nounced. VIF not only reduced the cytopathic effe of polioviruses on human amnion and human kidn cells but also reduced the yield of virus. VIF did n appear to inhibit adsorption but it probably had son effect upon the spread of virus from cell to cell as we as a reduction in the yield of poliovirus. One of th original observations made with RMC virus was th when inoculated into amnion or kidney cultures in hig concentration a prozone phenomenon occurs in th the cytopathic effect at high concentrations is conside ably less than it is nearer the infectivity end-poir It seems that this prozone is probably due to the pr sence of VIF because (a) RMC virus separated fro the accompanying VIF by ultracentrifugation does n give rise to prozone and chronic infection; (b) th responsible factor like VIF is destroyed by trypsi (c) fluids taken from the prozone when freed fro infectious virus by antibody or ultracentrifugatio reveal the presence of VIF by inhibiting all 3 typ of poliovirus.

A chronic infection of a strain of HeLa cells wi RMC virus was also established. In the system on a few of the HeLa cells were infected but the vir and the cells were carried together for a period of months. In this system it was found that VIF r cognized by its inhibitory effect on poliovirus infectio of human amnion or kidney cells was present but th presence of VIF could not be recognized by challeng experiments in HeLa cells. Similarly, VIF prepared human kidney cultures did not prevent the cytopath effect of polioviruses in HeLa cells. The authors no that their VIF has many of the properties of interfer described by ISAACS and LINDEMANN [*ibid.*, 1957, 32, 1203, *bis*]. It is a product of the interaction of viru and host cells and the chemical and physical properti of the 2 substances are similar, but certain differenc are noted: (1) VIF is optimally produced with activ virus whereas interferon is produced with inactive viru (2) VIF is adsorbed poorly if at all to cells where interferon is readily adsorbed. (3) VIF acts mo effectively when it is continually present in the syste whereas interferon after adsorption to the cells m then be removed. (4) Interferon (supplied by Dr. ISAAC and prepared in chick embryo tissues) does not inhib type 1 poliovirus infection in amnion cultures. It seem probable that a variety of inhibitory substances simil to interferon are formed as a result of different viru host interactions.

[This is a very long and detailed paper containin

important and interesting results. It deserves to be read in the original. The lack of an effect of interferon prepared in chick embryo tissues on poliovirus infection of human amnion cells may not be very significant in view of the apparent host specificity of interferon [ISAACS and WESTWOOD, *ibid.*, 1960, v. 35, 320].] *A. J. Beale*

ALIVISATOS, G. P. & EDIPIDIS, T., with the technical collaboration of M. VARDALA & G. PAGOULATOS. **On the Immunization of Cells in Cell Cultures. I. Communication.** *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Dec., v. 118, No. 6, 427–41, 9 figs. [14 refs.]

It was found that if human amnion tissue cultures were "vaccinated" with a 1:20 dilution of killed poliovaccine (the final dilution was 1:100) and then about 10 days later were challenged with 100 TCD of type 1, 2 or 3 poliovirus no specific cytopathic effects due to poliovirus were noted. No protective effect occurred if virus and vaccine were given simultaneously or when there was an interval of 12 hours between adding the vaccine and challenge with live virus. The fluid from successfully vaccinated cells was found to neutralize 50 TCD of poliovirus of all 3 types when mixed together and held at 37°C. for 1 hour, and then the mixture was inoculated into susceptible cells. From these experiments it is concluded that after inoculation of human amnion tissue cultures with killed poliovaccine neutralizing substances appear in the tissue culture system after about a week. The virus inhibitory effects are not ascribed to viral interference or to the appearance of interferon, because of the long delay in the appearance of the neutralizing substance.
A. J. Beale

GRODUMS, E. Irene & DEMPSTER, G. **The Age Factor in Experimental Coxsackie B-3 Infection.** *Canadian J. Microbiol.* Ottawa. 1959, Dec., v. 5, No. 6, 595–604, 10 figs. (8 on 2 pls.) [43 refs.]

An investigation is presented of the varying susceptibility with age of an inbred strain of mice, originally derived from the Connaught Medical Research Laboratories, Toronto, infected with Coxsackie B type 3 (Nancy strain) virus. This was a large scale and elaborate investigation in which groups of at least 10 mice at various ages were used for histological and also the same number for virological studies. The mice were inoculated intracerebrally with about $10^{4.5}$ LD50 of the Coxsackie B3 virus. Clinical disease occurred in almost all mice inoculated at 1 or 4 days but in only one-third at 7 days and was very rare in mice of 9 or 12 days. In mice under 4 days old, lesions in the brain were severe and almost universal, but these decreased rapidly with age and by 15 days were no longer observed in any mice. By contrast lesions in the heart were not seen in mice under 4 days but first appeared in 7-day-old mice and increased in incidence and severity to reach a peak between 17 and 23 days and thereafter occurred in the majority of mice but were less severe. Lesions in the brown fat were extensively studied. These were severe up to the age of about 26 days but thereafter were rather less severe.

The character of the lesions of the brown fat fell into 3 groups based upon the age of the mice. In newborn to 12-day-old mice the periphery of the lobules showed extensive necrosis and a slight inflammatory response and the centre of the lobules contained cells with a decreased number of lipid granules and some granulation tissue. In the second group, from 17 to 26 days old, the periphery of the lobules also showed necrosis but the centre of the lobules showed cells with enlarged lipid globules and also some necrotic cells. In older mice the periphery of the lobules showed no necrosis but some necrotic cells in the centre of the lobules and enlarged lipid globules. The exact significance of the changes in the lesions in the brown fat is at present unknown but it is thought that it may be related to the other changes in age susceptibility. Viraemia was almost universal in animals inoculated at 4 days but was not found in animals aged 9 days or more. The virus was also isolated from brain, brown fat and hearts of animals showing lesions.
A. J. Beale

GRODUMS, E. Irene & DEMPSTER, G. **Myocarditis in Experimental Coxsackie B-3 Infection.** *Canadian J. Microbiol.* Ottawa. 1959, Dec., v. 5, No. 6, 605–15, 8 figs. (7 on 2 pls.) [35 refs.]

In the foregoing paper one of the most striking features was the appearance of severe myocardial lesions in mice infected with Coxsackie B3 virus over the age of 4 days. Previously this finding has not been very frequently observed except in mice treated with cortisone (see, for example, KILBOURNE *et al.*, *J. Lab. Clin. Med.*, 1953, v. 42, 826). In view of the recently described fatal myocarditis in newborn babies and also of the association of pericarditis with Coxsackie B virus infection in older individuals the factors involved in myocardial lesions in mice were more fully examined [see, for example, NAUDE *et al.*, this *Bulletin*, 1959, v. 34, 28 and MCLEAN *et al.*, *Canadian Med. Assoc. J.*, 1958, v. 79, 789]. Again the Nancy strain of Coxsackie B3 virus was used given either intracerebrally or subcutaneously and it was confirmed that myocardial lesions very similar to those seen in fatal human cases occurred in suckling mice. The lesions were most severe in mice aged 12 and 17 days but were also universally found in sexually mature mice although their severity was considerably less. The effect of this strain of Coxsackie virus was about the same with $10^{4.5}$ or $10^{2.0}$ LD50 as inoculum.

In the initial experiments all the mice had been killed 7 days after inoculation of Coxsackie virus and it was found that the lesions were more frequent and more severe when the animals were killed at this time than if they were allowed to live for 14 or 28 days. Lesions were slightly more severe if tissue culture supernatant fluids were employed as inoculum instead of the more usual carcase suspension. The original inbred strain of mice appeared to be more susceptible to myocardial lesions than the Albany strain of mice that has been used in the extensive work on Coxsackie viruses by Dr. DALLDORF and his colleagues. Using the

Albany strain, although lesions were quite frequent, they were usually very small. Crossing of the authors' inbred strain of mice with a wild mouse gave rise to mice of almost equal susceptibility to myocardial lesions. Lesions were slightly more severe in male than in female mice. No myocardial lesions were found in 95 normal mice examined at various ages nor in adult mice inoculated with virus plus specific antiserum. However, 5 out of 19 adult mice inoculated with a 1/100 dilution of normal mouse carcase suspension showed typical myocardial lesions. Coxsackie B3 virus was regularly obtainable from the hearts of mice with lesions following the inoculation of Coxsackie B3 virus but not from any of the control mice including those showing lesions following the inoculation of carcase material. The histological features of the myocardial lesions are illustrated. The predominant lesion was hyaline degeneration and necrosis of heart muscle fibres but periarteritis was also observed and also fibrosis and invasion by mononuclear cells.

A. J. Beale

SICKLES, Grace M., MUTTERER, Marie & PLAGER, Hildegard. **New Types of Coxsackie Virus, Group A. Cytopathogenicity in Tissue Culture.** *Proc. Soc. Exper. Biol. & Med.* 1959, Dec., v. 102, No. 3, 742–3. [10 refs.]

Details of 5 new Coxsackie A types are described and numbered A 20, 21, 22, 23 and 24. All the prototype strains cause myositis and flaccid paralysis in newborn mice, but other strains of A 23 normally known as ECHO 9 rarely cause lesions in suckling mice directly from the patient [EGGERS and SABIN, this *Bulletin*, 1960, v. 35, 406]. A 23 and A 9 have been shown to cross-react in complement-fixation tests by TYRRELL *et al.* [*ibid.*, 1958, v. 33, 803] but do not cross in neutralization tests. The strains were also tested in tissue cultures of monkey kidney, human uterine, HeLa, human amnion and chick embryo cells. A 22 and 24 did not produce any cytopathic effects. A 20 produced cytopathic effects only in HeLa cells (the effect was more pronounced in some strains of HeLa cells than in others). A 21 produced effects in human uterine, amnion and HeLa cells, whilst A 23 produced effects in monkey kidney and human amnion cells. 3 strains of A 20 were studied which differed slightly in antigenicity although sharing major neutralizing antigens.

A. J. Beale

KARZON, D. T., POLLOCK, Beatrice F. & BARRON, A. L. **Phase Variation in ECHO Virus Type 6.** *Virology.* New York. 1959, Dec., v. 9, No. 4, 564–76, 1 fig. [16 refs.]

It has frequently been observed that new isolates of ECHO viruses are poorly neutralized by antiserum to the prototype ECHO virus but that antiserum to the new isolate satisfactorily neutralizes the prototype strain. Such ECHO strains giving a one-way cross neutralization with prototype ECHO strains have been called "prime" strains (MELNICK, *Ann. N.Y. Acad. Sci.*, 1957, v. 67, 363). Such ECHO 6 prime strains have been isolated by KARZON *et al.* from an epidemic abacterial meningitis in Buffalo in 1955 [this *Bulleti* 1957, v. 32, 388]. Now an analysis of 11 strains h been undertaken. It was found that strains could divided into 3 groups or phases. The titre of antiseru inhibiting 100 TCD50 of homologous virus when re 48 hours after degeneration of the cells in the vir control was called 1 unit.

(1) Specific (S) phase. The virus required 10–1 units of heterologous antiserum to neutralize it, *i.e.* t titre against heterologous antisera with these S strai was much less than with the homologous strain.

(2) Broad (B) phase. These were neutralized by unit of all the antisera.

(3) Intermediate phase. These strains required b tween 5 and 20 units of heterologous antiserum neutralize them.

The classification of a strain varied slightly dependi upon the sera used. Thus a strain Benson would ha been considered to be in the S phase with Troy an Shobaken antisera and in the B phase with Rigg and Roth antisera. In general S phase viruses had le passages in monkey kidney culture, lower titres an less rapid destruction of the cells. On passage monkey kidney they tended to become B phase. T S phase viruses tended to show a break through of t neutralizing ability of the serum. Thus for B pha viruses the titre of a serum at the onset of degener tion of the control cultures and 48 hours later wh the results were read was slight, whereas for S pha serum the titre may have dropped 100-fold in th 48-hour period.

[See also NEVA *et al.*, below.] *A. J. Beale*

NEVA, F. A. & MALONE, Mary F. **Specific and Cro Reactions by Complement Fixation with Bostc Exanthem Disease Virus (ECHO-16).** *J. Immun logy.* 1959, Dec., v. 83, No. 6, 645–52. [18 refs.

The aetiological agent of Boston exanthem disea [NEVA, this *Bulletin*, 1956, v. 31, 1065 and NEVA an ZUFFANTE, *ibid.*, 1958, v. 33, 212] has been shown to antigenically related to ECHO type 16 virus. A stu of the usefulness of the complement-fixation reactio has been made with 2 strains (Clauss and V. Floy from the Boston cases and 2 strains (Nickolas an McGrew) from the Pittsburgh outbreak. The virus were grown on plasma clot cultures of human foreski and before use as complement fixing (CF) antigens ha to be concentrated either by ultrafiltration or by dialy against polyvinyl-pyrrolidone. With 2 lots of patien sera and the sera from immunized monkeys it w found that the 4 strains of Boston exanthem vir appeared the same. Most of the sera from the patien with Boston exanthem disease showed a rise complement-fixing antibody titre during the disea However, titres over 1 in 8 sera found quite frequently sera collected from various persons in Boston an Pittsburgh, roughly 50% of those over 4 years of a contained these antibodies. There appeared to be ve little correlation between the incidence of complemen fixing antibodies to Boston exanthem virus and neutr lizing antibodies. Similarly, with a variety of pair

era from patients infected with a range of enteroviruses epresenting ECHO 2, 6, 9, 20 and Coxsackie B1 and 3, it was found that complement-fixing antibodies to the Boston strains were extremely prevalent. The authors note that several previous investigators have found that the complement-fixation test reveals extensive cross reactions within members of the enterovirus group. See for example, VON ZEIPEL and SVEDMYR, this *Bulletin*, 1957, v. 32, 1137.] *A. J. Beale*

NEVA, F. A., MALONE, Mary F. & LEWIS, L. J. **Antigenic Comparison of Boston Exanthem Virus Strains and their Relationship to ECHO-16 Virus as studied by Neutralization and Complement Fixation Procedures.** *J. Immunology*. 1959, Dec., v. 83, No. 6, 653–60, 3 figs. [15 refs.]

In this paper 5 strains of Boston exanthem virus are compared with the Harrington strain of ECHO 16 virus in cross neutralization and complement-fixation tests. It was found in general that all the strains shared antigenic characters, but nonetheless distinct antigenic differences were noted especially between individual strains of the Boston exanthem viruses. In this study plasma clot cultures of human skin and muscle were used because of their greater sensitivity than monkey kidney cells to minimal amounts of Boston exanthem virus. It was found, however, that the viruses tend to break through the antisera on prolonged incubation and this led to a method of recording the results as a profile of the titre recorded at daily intervals and it is mainly as a result of this technique that the differences in antigenic character between strains were suggested. The authors note that the method of growing the virus used to prepare specific antisera, the nature of the course of injections and the characters of the virus antigen used in the test, all affect the results of an antigenic analysis. The results of this study confirm that the Boston exanthem strains should really be considered as members of the ECHO 16 type although the clinical features of the disease associated with the prototype ECHO 16 strain (abacterial meningitis) and from the Boston exanthem strains are dissimilar.

A. J. Beale

GAIDAMOVICH, S. I. & DESIATKOVA, R. G. **Attempts to Cultivate the Virus of Infective Hepatitis in Tissue Cultures.** *Problems of Virology*. London. 1958, v. 3, Nos. 5/6, 335–7. [Translated from Russian.]

"(1) Attempts were made to isolate hepatitis virus from the blood and faeces of patients suffering from hepatitis and from the spleen and liver of patients who had died of the disease, and to cultivate the virus in tissue cultures of human embryo liver, kidney, spleen and muscle tissue. Twenty-nine different materials were investigated through 2–13 passages.

"(2) Attempts to establish the multiplication of a virus in the cultures by morphological studies (detection of a cytopathogenic effect), by complement-fixation tests and by estimation of aldolase activity led to negative results."

ADAMCOVÁ, J. & BÁRDOS, V. **Notes on the Study of the Ecology of Viruses of the Col SK Group.** *Acta Virologica*. Prague. 1959, Oct., v. 3, No. 4, 234–9. [22 refs.]

KARSTAD, L. & HANSON, R. P. **Natural and Experimental Infections in Swine with the Virus of Eastern Equine Encephalitis.** *J. Infect. Dis.* 1959, Nov.–Dec., v. 105, No. 3, 293–6, 1 fig.

Neutralizing antibodies to eastern equine encephalitis virus were previously demonstrated in swine in Georgia and New Jersey. In tests in the allantoic cavity of eggs, 8 of 43 swine from Wisconsin were shown to have log neutralizing indices of 1·8–3·0. 15 pigs without naturally occurring antibody were experimentally infected intranasally with 10^6LD50, intradermally with 10^2–10^6LD50, intravenously with 10^2 and 10^6LD50 and intracerebrally with 10^2LD50. None showed symptoms and virus was not isolated from brain, liver, spleen or kidney of 4 examined. Histological evidence of encephalitis was found in 1 pig inoculated intradermally: this animal had concurrent diarrhoea during the experiment. All the pigs experimentally infected developed neutralizing antibody (1·6–3·7 log). 2 uninoculated animals were kept in contact with the experimentally infected animals, but they showed no symptoms or antibody response. *C. E. Gordon Smith*

TRAUB, E. & SCHWÖBEL, W. Über die Immunität der weissen Maus gegenüber dem EEE-Virus. III. Mitteilung: Versuche zum Nachweis von aktivem Virus bzw. Virusantigen in den Organen immuner Mäuse. [**Immunity of the White Mouse to Eastern Equine Encephalomyelitis Virus. III. Attempts to Demonstrate Active Virus or Virus Antigen in the Organs of Immune Mice**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Aug., v. 118, No. 2, 86–102. [13 refs.]

The authors have attempted to detect the persistence of virus in mice possessing active immunity to eastern equine encephalomyelitis. No recrudescence of the virus infection could be observed in 508 immune mice which were observed until the end of their natural lives, and no infectious virus could be demonstrated by intracerebral passage in the brains of 386 old immune mice, or by culturing the tissues of immune animals. A procedure for concentrating virus from the organs of recently infected mice by means of adsorption on aluminium hydroxide and subsequent elution was developed, but it was not possible by this means to detect specific antigen in the tissues of immune mice.

[See also this *Bulletin*, 1959, v. 34, 1195.]

D. J. Bauer

CLARKE, D. H. **Antigenic Analysis of Certain Group B Arthropod-Borne Viruses by Antibody Absorption.** *J. Exper. Med.* 1960, Jan. 1, v. 111, No. 1, 21–32, 1 fig. [18 refs.]

A 20% suspension of infected mouse brain in *p*H 9·3 buffered saline was spun at 11,000 r.p.m. for 1 hour.

The supernatant was then spun at 40,000 r.p.m. for 2 hours and the resultant pellets were used to absorb sera by resuspending them in the serum, incubating the mixture overnight at 4°C. and then centrifuging again at 40,000 r.p.m. for 2 hours. Absorbed and unabsorbed sera were then absorbed with kaolin and goose cells before testing. The absorbing efficiency of virus suspensions was not clearly correlated with their haemagglutinin activity. Attempts to use virus-coated erythrocytes for absorptions were unsuccessful.

When immune serum was absorbed with increasing amounts of the homologous virus the homologous haemagglutinin-inhibiting (HI) titres fell, giving a curve with a slope varying with the virus used. Different viruses differed in their absorbing efficiency, but no variation was found between different preparations of the same virus. When an immune serum was absorbed with increasing amounts of a heterologous virus (*e.g.* St. Louis serum with yellow fever virus) the homologous HI antibody showed some fall, then remained constant regardless of the amount of virus used. In subsequent studies enough absorbing virus was used either to remove all antibody or to reduce it to the constant level.

3 strains of West Nile virus were compared (from Uganda, Egypt and India). When enough of any of them was used it absorbed all the antibody from antisera to the Egypt and India strains. They thus appear to be antigenically identical. Antigens from the Uganda strain gave higher HI titres than from the other 2; differences in reactivity with antibody therefore exist.

Antisera to dengue-1 (Hawaii), dengue-2 (New Guinea B) and dengue (Trinidad 1751) were absorbed with West Nile virus (Egypt 101). The sera were tested for HI antibody to these viruses and to an Indian dengue virus (P8640). The heterologous antibodies were removed, but homologous antibodies were only slightly affected. The dengue viruses were shown to be related by 1 or more shared antigens not present in West Nile and the Trinidad and India strains were shown to be strains of dengue-2.

Viruses of the Japanese-encephalitis—St.-Louis—West-Nile subgroup (JE, SLE, WN, Murray Valley (MVE), Ilheus) were compared by absorption of SLE and JE sera with all 5 and with yellow fever virus. All heterologous antibody was removed from SLE serum by WN, MVE and JE, and from JE serum by WN and MVE. Only MVE antibody remained after absorption of JE serum with SLE, and MVE and JE are known to be very closely related. Ilheus, however, did not absorb all antibody to WN and MVE from SLE serum, nor all MVE, WN and SLE antibody from JE serum; Ilheus is thus less closely related than the other members in the subgroup. Yellow fever virus absorbed all the antibody only to Ilheus and yellow fever in the JE and SLE sera and only to JE and yellow fever in Ilheus serum.

Yellow fever serum prepared with the French strain (Africa, 1928) was absorbed with 4 other African strains (French neurotropic, Asibi, 17D, Ogbomoshe) and 3 American strains (BeH70, Tr4754, JSS). The African strains absorbed all the antibody while all the American strains failed to remove antibody reacting with African antigens, but removed antibody reacting with American antigens. African strains appear to have an antige which is absent in American strains. 17D virus is a attenuated variant of Asibi and when 17D serum w absorbed with Asibi virus all the HI antibody to 17 was not removed. Thus 17D has acquired an antige not present in its parent strain. The significance of th important study in the classification of arboviruses discussed. *C. E. Gordon Smith*

KUNDIN, W. D. & DIERCKS, F. H. **Demonstration Japanese Encephalitis Virus Hemagglutinin i Hamster Kidney Cell Culture Fluids.** [Corr spondence.] *Virology. New York.* 1960, Jan., 10, No. 1, 153–5.

OHYAMA, A., ISHIGA, A., FUJITA, N., AOKI, H., YAMAD T. & HOTTA, S. **Effect of Human Gamma Gl bulin upon Encephalitis Viruses.** *Japanese Microbiol.* 1959, Apr., v. 3, No. 2, 159–69, 7 fig [23 refs.]

2 strains of Japanese encephalitis and 1 of St. Lou encephalitis virus, all after over 100 mouse passage were used. Gamma globulin from Japanese subjec was used. The gamma globulin was cytotoxic for chic embryo cells at a concentration of 10% but not at 1% L strain fibroblasts were affected at 1% but not at 0·1% In intracerebral neutralization tests in mice, the gamm globulin gave log neutralizing indices of 2·0–2·75 again Japanese encephalitis, but no neutralizing antibo against St. Louis virus was detected. When mice give varying doses of Japanese encephalitis virus intr cerebrally were given 0·1 ml. of gamma globulin intr muscularly 24 hours later, the mice were protecte against up to about 100 LD50. There was less eviden of protection when the gamma globulin was given aft an interval of 48 hours. No protection was achieve against St. Louis virus. 3 groups of 30 mice we given about 100 LD50 of Japanese encephalitis vir intraperitoneally: 1 group received 0·1 ml. of gamm globulin 24 and 48 hours later, another received norm serum, and the third no treatment. 20 mice survive in the first group, 16 in the second group and 10 the third. [The authors state that a significant diffe ence at the 5% level was demonstrated between the groups, but such a difference appears to exist on between the first and third groups.] Mice inoculate intracerebrally with about 100 LD50 of Japane encephalitis virus were given 2 doses of 0·1 ml. gamma globulin at varying intervals after infectio The mortality ratios of mice treated 1 and 2 day 2 and 3 days, 3 and 4 days and 4 and 5 days aft infection, were 2/15, 4/15, 2/15, 3/15 respective compared with 20/28 untreated mice.

Gamma globulin from a country where Japane encephalitis frequently occurs apparently contains signi cant amounts of neutralizing antibody and may have therapeutic effect if given soon after infection (*i.* during the incubation period) in mice. [This paper difficult to evaluate as most of the results are pr sented in diagrams from which exact figures a difficult to derive.] *C. E. Gordon Smith*

LIU, Yuan-Yuan. [**Studies of the Method for preparing Japanese B Encephalitis Vaccine. II. Dynamics of the Inactivation of the Effective Dose and Concentration of the Mouse Brain Vaccine.**] *Acta Microbiologica Sinica.* 1959, Dec., v. 7, No. 4, 319–26, 1 fig. [20 refs.] [In Chinese.]

The English summary appended to the paper is as follows:—

"The dynamics of inactivation of Japanese B encephalitis virus (Peking strain) by the action of formaldehyde was studied. It was shown that the inactivation curves, no matter by what means drawn, were not straight lines, and either in a 10% centrifuged mouse brain suspension or in a 2% diluted centrifuged suspension. The results were the same. Whether the inactivation is a multimolecular reaction or a monomolecular reaction is discussed in the paper.

"The experiment showed that the concentration of formaldehyde used would influence the protective titre of the vaccine, higher concentration of formaldehyde lowered the protective titre. A proper concentration of formaldehyde to be used for the preparation of this vaccine was therefore mentioned.

"When the vaccine prepared from the uncentrifuged 10% mouse brain suspension was first centrifuged at low speed and then diluted 5 times, there was no difference between the protective titres of these two vaccines. The possibility of eliminating the allergic factors by means of centrifugation and dilution was also discussed.

"The results of this experiment also showed that when carbolic acid was used as the antiseptics, the prepared vaccine would show a higher protective titre than when phenylmercuric nitrate was employed."

ANGELILLO, B. & MASIA, G. F. Ulteriori ricerche sul potere emoagglutinante di alcuni virus Arbor. [**Further Researches on the Haemagglutinating Power of some Arbor Viruses**] *Igiene Moderna.* 1959, v. 52, Nos. 7/8, 449–57, 1 graph.

The English summary appended to the paper is as follows:—

"A new series of researches has been carried out on the haemagglutinating power of some viral agents transmitted by Arthropods.

"Strains of Ilheus, Ntaya, Uganda S viruses, used in the present researches, failed to show any haemagglutinating activity at any *p*H and temperature. Sindbis virus agglutinated red blood cells of newborn chickens, with highest titres at *p*H 6·4–6·7 at 4°C, and *p*H 6·6–6·7 at 37°C.

"The haemagglutination was inhibited by the homologous antiserum and, at lower titres, by the anti-Semliki serum of the same A group. It was inhibited by antisera prepared with viruses of the B group (Ilheus, Ntaya, Uganda S)."

MATUMOTO, M., NISHI, I. & SABURI, Y. Interférence chez la souris de la souche neurotrope avec la souche pantrope du virus de la fièvre de la Vallée du Rift. [**Interference in Mice by the Neurotropic with the Pantropic Virus of Rift Valley Fever**] *C.R. Soc. Biol.* 1959, v. 153, No. 10, 1634–8, 1 fig.

MATUMOTO, M., NISHI, I. & SABURI, Y. Conditions nécessaires pour l'interférence du virus neurotrope avec le virus pantrope de la fièvre de la Vallée du Rift. [**Conditions Necessary for Interference by Neurotropic with Pantropic Virus in Rift Valley Fever**] *C.R. Soc. Biol.* 1959, v. 153, No. 10, 1645–8.

MATUMOTO, M., NISHI, I. & SABURI, Y. Interférence dans la fièvre de la Val.ée du Rift. Influence de la souche neurotrope sur la multiplication de la souche pantrope. [**Interference in Rift Valley Fever. Influence of the Neurotropic Strain on the Multiplication of the Pantropic Strain**] *C. R. Soc. Biol.* 1959, v. 153, No. 10, 1649–52, 1 fig.

MATUMOTO, M., NISHI, I., SABURI, Y. & SUZUKI, T. Interférence dans la fièvre de la Vallée du Rift chez la souris. Interférence de la souche neurotrope irradiée avec la souche pantrope. [**Interference in Rift Valley Fever in Mice. Interference by the Irradiated Neurotropic Strain with the Pantropic Strain**] *C.R. Soc. Biol.* 1959, v. 153, No. 10, 1657–9, 2 figs.

MATUMOTO, M., NISHI, I. & SABURI, Y. Interférence dans la fièvre de la Vallée du Rift chez la souris. Effet de l'ultracentrifugation sur le pouvoir inhibiteur de la souche neurotrope. [**Interference in Rift Valley Fever in Mice. Effect of Ultracentrifugation on the Inhibitory Power of the Neurotropic Strain**] *C.R. Soc. Biol.* 1959, v. 153, No. 10, 1664–5.

MUTAI, M. **Isolation and Identification of Measles Virus.** *Japanese J. Exper. Med.* 1959, Aug., v. 29, No. 4, 283–95, 18 figs. on 2 pls. [25 refs.]

"Four strains of measles virus which occurred in Tokyo in 1957 and 1958, were isolated in cultures of trypsinized monkey kidney cells from throat swabs of patients. The strains were identified by comparing them with the Edmonston strain of measles virus by neutralization and complement fixation tests and by cytopathogenic effect in monkey kidney cell cultures. This was further confirmed by neutralization and complement fixation tests with pairs of acute and convalescent sera of measles patients.

"This is the first report in Japan that describes the isolation of measles virus in cell cultures.

"The behavior of the Sugiyama strain, one of our isolates, was described in cultures of several human cell strains. The findings indicate the general utility of these cell strains for investigation on measles virus."

CABASSO, V. J., KISER, K. H. & STEBBINS, M. R. **Distemper and Measles Viruses. I. Lack of Immunogenic Crossing in Dogs and Chickens.** *Proc. Soc. Exper. Biol. & Med.* 1959, June, v. 101, No. 2, 227–30. [14 refs.]

The relationship between measles and distemper viruses [this *Bulletin*, 1957, v. 32, 1131; 1959, v. 34, 13]

has been further investigated in cross-neutralization tests. 6 puppies vaccinated with the CD strain of canine distemper virus developed homologous neutralizing antibody after 4 to 5 weeks in titres of 940–1,600, but no neutralizing or complement-fixing antibodies to the Edmonston strain of measles virus could be detected. A similar absence of cross-reaction was also observed in 2 groups of 6 roosters immunized with distemper and measles viruses respectively. *D. J. Bauer*

RAPP, F., SELIGMAN, S. J., JAROSS, Lorene B. & GORDON, I. **Quantitative Determination of Infectious Units of Measles Virus by Counts of Immunofluorescent Foci.** *Proc. Soc. Exper. Biol. & Med.* 1959, June, v. 101, No. 2, 289–94, 2 figs. [11 refs.]

The authors have developed a method of carrying out particle counts of the Edmonston strain of measles virus, which does not form plaques, by the fluorescent antibody method. Sheets of Hep-2 cells grown on coverslips in plates were exposed to virus for 2 hours, covered with an overlay of 2% methyl cellulose and 20% horse serum in Eagle medium, and then incubated for 3–6 days in a sealed desiccator in which a candle had been allowed to burn out to provide carbo dioxide. The overlay was then liquefied by cooli to 4°C. for 1 hour and decanted. The coverslips we washed several times with cold phosphate-buffere saline, fixed with acetone for 10 minutes at roo temperature and then examined by fluorescence micr scopy with human convalescent-phase measles an serum and fluorescein-labelled antihuman globul horse pseudoglobulin. Fluorescent foci appeared aft 12 hours incubation, and after 5 days they were mul cellular and could easily be counted with a magnific tion of 100 diameters. The method gave goo quantitative results and agreed well with the resul of tube titrations. *D. J. Bauer*

NIKOLITSCH, M., GILDEMEISTER, H. & JELESITSCH, Die Vermehrung des Tollwutvirus in einem für d Tollwut nicht empfänglichen Tierorganismus. [**Th Multiplication of Rabies Virus in an Anim insusceptible to Rabies**] *Arch. f. Hyg. u. Bak* 1959, Aug., v. 143, No. 5, 357–65, 2 figs. [11 refe

[An abstract of this paper appeared in the *Tropic Diseases Bulletin*, 1960, v. 57, 466.]

IMMUNITY

SCHAEDLER, R. W. & DUBOS, R. J. **Effect of Dietary Proteins and Amino Acids on the Susceptibility of Mice to Bacterial Infections.** *J. Exper. Med.* 1959, Dec. 1, v. 110, No. 6, 921–34.

The authors show that both qualitative and quantitative differences in protein and amino-acid nutrition are of importance in the response of young mice to induced bacterial disease.

The authors used in their experiments diets which comprised a protein-free mixture containing all the known growth factors and supplemented with cystine, to which was added one of the following: varying amounts of casein or gluten, gluten + lysine, or soybean α protein. Commercial food pellets and a soybean-rice-flour mixture were also used in the experiments. Food (*i.e.* a specific diet) and water were supplied *ad lib* to the animals in all experiments.

The authors studied the effects of these diets on the weight of young mice, and on the response to infection produced by the intravenous administration of one of the following pathogens: *Staphylococcus aureus*, *Mycobacterium tuberculosis* var. *bovis*, *Mycob. fortuitum*, and *Klebsiella pneumoniae*, Type C.

The resistance to infection shown by mice on different diets were compared by studying the cumulative deaths at given intervals. The observed differences in resistances were maintained when the airborne or intraperitoneal route of infection was used.

The authors found that mice given diets containing 15% or 20% casein were more resistant to infection and gained weight more satisfactorily than those given diets with 5% or 8% casein, 15% or 20% gluten, or 15% or 20% soybean protein.

They found a marked difference in weight gain, b no difference in resistance to infection, between mi fed 8% casein and mice fed 5% casein in their diet they also found that supplementation of gluten die with lysine improved weight gain but did not enhan resistance to infection.

Where mixed plant proteins with an amino-ac content similar to that of casein (soybean-rice-flo mixture) were used in a diet at a concentration 15%, satisfactory weight gain and resistance to infe tion were noted.

The authors repeated one of their experiments wi a second strain of mice differing in natural resistan to bacterial infection and obtained consistent results.

The authors conclude that the relative proportion the various amino-acids in the diet is as importa as their total amount in conditioning resistance bacterial infection and that this effect of nutrition c resistance is independent of the route of infectio whether intravenous, intraperitoneal, or airborne.

[For an earlier study by the authors, see this *Bulleti* 1958, v. 33, 1195.] *Frank Russell*

DUBOS, R. J. & SCHAEDLER, R. W. **Effects of Nutritio on the Resistance of Mice to Endotoxin and o the Bactericidal Power of their Tissues.** *J. Expe Med.* 1959, Dec. 1, v. 110, No. 6, 935–50.

The authors followed up the results of the work i the preceding paper by describing the fate of infectiv organisms in the tissues of mice given different experi mental diets, and the ability of the mice to resist th toxic effects of infection. The experimental diets wer

as described in the preceding paper. Corn grain was also used as a sole source of food.

Mice given a complete diet were found resistant, and mice fed on defective diets, susceptible, to coagulase-negative *Staphylococcus albus*. However, mice given defective diets cleared their tissues (blood, liver, spleen, lung, kidney) of organisms as efficiently as did those fed on a complete diet (estimated by quantitative techniques applied to the organs of mice killed at intervals after infection).

The authors repeated this type of experiment using *Staph. aureus* and virulent *Klebsiella pneumoniae*, and found that although undernourished mice succumbed rapidly to infection, the bactericidal power of their tissues was remarkably unaffected.

Mice given various diets were infected by the intravenous inoculation of a coagulase-positive *Staph. aureus* in combination with an endotoxin prepared from either *Serratia marcescens* or *Escherichia coli*. Mice on deficient diets died rapidly under this treatment but before death they retained the ability to eliminate organisms from their tissues.

The lethal dose of endotoxin alone was found to be much smaller for mice on inadequate diets. Mice fed on corn grain only were particularly susceptible to the lethal effects of endotoxin. Since the animals lost weight markedly on this regime, the authors compared the LD50 of endotoxins from *K. pneumoniae* and *E. coli*, for mice fed on corn, and mice fed on commercial pellets. They found that the increased susceptibility to endotoxin of mice on deficient diets could not be explained on weight differences alone.

Since a large proportion of mice fed on defective diets died shortly after the simultaneous injection of avirulent *Staph. albus* and endotoxin, and since the same number of heat-killed cocci had no effect, it is suggested that the toxaemia may be an expression of a heat-labile toxin, or the metabolic activities of the bacteria.

In the final experiments it is shown that simultaneous injection of bacteria and endotoxin can be used as a test of the nutritional state of the animals.

The authors conclude, as a result of their experiments, that the nutritional state influenced the outcome of infection by diminishing the ability of the mice to resist the toxic effects of bacteria, rather than by affecting the fate of the bacteria *in vivo*.

Frank Russell

HENON, Michelle; PELLETIER, Monique; DELAUNAY, A. Substances antibactériennes d'origine tissulaire. I. Pouvoir agglutinant de certains polypeptides basiques [HENON, PELLETIER & DELAUNAY]. [**Antibacterial Substances of Tissue Origin. I. Agglutinating Property of Certain Basic Polypeptides.**] *Rev. d'Immunologie*. 1959, July–Sept., v. 23, No. 4, 245–57, 1 fig. II. Pouvoir opsonisant de certains polypeptides basiques [PELLETIER, HENON & DELAUNAY]. [**II. Opsonising Property of Certain Basic Polypeptides**] *Ibid.*, 258–72, 4 figs.

I. The authors describe the agglutinating power, for different species of bacteria, of certain substances extracted from calf liver and thymus. There is a detailed description of 6 methods employed for the extraction of these substances from tissues. The purified extracts had all the properties of basic polypeptides.

Solutions of the polypeptides (2 mgm./ml.) were mixed with suspensions of organisms in physiological saline (approximately 5,000 million cells/ml.) in proportion of 2 volumes to 1. The mixtures were held at room temperature for 2 hours. The bacteria examined, among others, were a pathogenic and a non-pathogenic staphylococcus, a pathogenic coliform and *Salmonella typhi*.

Both Gram-negative and Gram-positive, pathogenic and non-pathogenic organisms were agglutinated. The extent of agglutination varied from one polypeptide to another. The authors suggest that this may be due to the different methods of extraction from tissues. If the suspensions of bacteria were first washed in physiological saline, agglutination was slightly diminished. The *p*H of the suspending medium had no effect on agglutination, but it was inhibited by the addition of either $CaCl_2$ on $MgCl_2$. It is suggested that agglutination is caused by a combination of the basic polypeptide with the nucleic acids of the bacteria, and that this may in some way modify their reaction to phagocytosis.

II. In the work described above the authors discussed certain basic polypeptides which were capable of agglutinating suspensions of Gram-positive and Gram-negative bacteria. They suggested that this reaction was due to a modification of the bacterial surface. This paper describes experiments which investigate the possibility that such a modification will render bacteria more susceptible to phagocytosis.

Suspensions of guineapig phagocytes in Ringer solution, fresh guineapig serum, and heated guineapig serum (1 hour at 56°C.) were mixed with suspensions of either untreated bacteria, or bacteria which had been suspended in solutions of polypeptides for 2 hours. The mixtures were incubated at 37°C. for 1 hour and films prepared and stained by methylene blue.

The results obtained were variable, but on the whole it would appear that bacteria treated with basic polypeptides extracted from thymus tissue were more easily phagocytosed than untreated bacteria. Phagocytosis of some individual species of bacteria depended to some extent on whether the suspending medium was fresh or heated guineapig serum. It was thought that after the organisms had been treated with the polypeptides, very few remained viable.

The authors suggest that the opsonizing effect is caused by a coating of polypeptide round the bacterial cells. This superficial "skin" may be attached to the cell by links between the basic polypeptides and the nucleic acids or nucleoproteins of the bacterium. Other links may occur between the polypeptides and glucidolipid polypeptide complexes on the surface of the cell, and this may be the explanation particularly for Gram-negative organisms.

Pretreatment of cells with lysozyme did not increase phagocytosis and in some cases actually inhibited it. The authors suggest that the opsonizing effect of polypeptides and the inhibitory action of lysozyme are both manifestations of a modification of the surface of the bacterial cell.

May F. McCallum

KLEIN, P. G. & BURKHOLDER, P. M. **Studies on the Antigenic Properties of Complement. I. Demonstration of Agglutinating Antibodies against Guinea Pig Complement fixed on Sensitized Sheep Erythrocytes.** *J. Exper. Med.* 1960, Jan. 1, v. 111, No. 1, 93–106. [23 refs.] **II. Analysis of Specific Agglutinins against Certain Components of Guinea Pig Complement fixed on Sensitized Sheep Erythrocytes.** *Ibid.*, 107–17.

I. "Evidence is presented to show that guinea pig complement fixed on sensitized sheep red cells acts as a specific agglutinogen. Agglutinating antibodies that react with cell-fixed complement can be produced by immunizing rabbits with a complex of stromata-amboceptor-complement or with guinea pig serum globulin. These agglutinins can be removed by precipitation with guinea pig serum. They are, therefore, distinct from immunoconglutinins."

II. "Sheep erythrocytes sensitized with amboceptor and persensitized thereafter with guinea pig complement are agglutinated by rabbit anti-guinea pig globulin and by immune sera obtained by injection of rabbits with fixed complement. In this agglutination neither C′1 nor C′2 takes part. Fixed C′4 acts as an agglutinogen. An additional agglutinogen, distinct from C′4, was found on persensitized cells. This additional agglutinogen appears to be distinct from hemolytically active C′3."

INGRAM, D. G. **The Conglutination Phenomenon. XIII. *In vivo* Interactions of Conglutinin and Experimental Bacterial Infection.** *Immunology.* Oxford. 1959, Oct., v. 2, No. 4, 322–33, 9 figs. **XIV. The Resistance Enhancing Effect of Conglutinin and Immuno-Conglutinin in Experimental Bacterial Infections.** *Ibid.*, 334–45.

XIII. "Some interrelations between the conglutinating activity of the serum of an animal and experimental bacterial infection were investigated. The passive transfer of conglutinating activity was demonstrated. The level of this activity reaches a peak within 2 days after subcutaneous injection, then declines until no significant titres are demonstrable in 12 to 14 days. It is shown that infection of animals with *Salmonella typhimurium* causes a rapid reduction in the conglutinating activity of the serum immediately after challenge. Evidence is presented which indicates that the previous injection of conglutinin preparations enhances bactericidal activity of the mouse against *Salm. typhimurium.*"

XIV. "The effect of conglutinin and immuno-conglutinin preparations on the resistance of animals has been studied in seven bacterial infections. In six infections—*Salmonella typhimurium, Pasteurella septica, Klebsiella pneumoniae, Listeria monocytogenes, Streptococcus pneumoniae* and *Streptococcus pyogenes*—higher survival rates were demonstrated in mice previously injected with the conglutinin preparations.

"Infection with avirulent strains or non-pathogenic organisms in numbers large enough to cause death led to severe toxaemia against which the injection of conglutinin preparations failed to protect. Although the conglutinin preparations failed to protect against avirulent or unadapted strains, they did protect against virulent or adapted strains of the organisms.

"Experiments undertaken to define the protecti factor in the serum preparations indicate that the pr tective factor probably is the same as that which responsible for the conglutinating activity, conglutinin

ROWLEY, D. **The Role of Opsonins in Non-Speci Immunity.** *J. Exper. Med.* 1960, Jan. 1, v. 1 No. 1, 137–44, 2 figs. [16 refs.]

"A study of the recoveries of radioactivity, and viable bacteria following injection of P^{32}-labelled *E. c* into the mouse peritoneum, has indicated that t rapid decrease in viable bacteria which occurs largely due to peritoneal events, and not to the transpo of bacteria elsewhere.

"The serum from mice given lipopolysaccharid 48 hours previously, when used to pretreat bacte before intraperitoneal injection, was found to stimula phagocytosis to a greater extent than did pretreatme with normal serum. In addition, macrophages the selves were found to be affected by contact with lip polysaccharides, either *in vivo* or *in vitro* in such way as to promote their phagocytic abilities. It suggested that the provocation of non-specific immuni by bacterial lipopolysaccharides involves two fac at least; firstly, an increase in the opsonic capacity the serum, and secondly an increase in the inhere capacity of phagocytic cells to perform this function."

KLEIN, P. G. **Studies on Immune Hemolysis: Pr paration of a Stable and Highly Reactive Co plex of Sensitized Erythrocytes and the Fi Component of Complement (EAC'1); Inactivati of Cell-Fixed C'1 by some Complement Reagen** *J. Exper. Med.* 1960, Jan. 1, v. 111, No. 1, 77–9 5 figs. [12 refs.]

"The interaction of sensitized sheep erythrocy (EA) with guinea pig complement inactivated by tre ment with hydrazine or ether has been studied. both cases EA is converted into EAC′1. The hemoly reactivity of this complex with respect to a compleme reagent that contains C′4, C′2, and C′3 (R1) deca rapidly in the presence of hydrazine-treated compleme (R4) or decomplemented guinea pig serum, but not the presence of ether-treated guinea pig serum or saline. The rate of decay of EAC′1 is dependent the temperature, the reaction volume, and the amo of the inactivating reagent. The capacity of R4 and decomplemented serum to inactivate EAC′1 can markedly reduced by treatment with ether. The esse tial conditions for obtaining an optimally reacti EAC′1 consist in exposing EA to ether-treated guinea p serum in the cold. This procedure yields a hig reactive EAC′1, even when the cells are sensitized w sub-optimal amounts of amboceptor."

ROZANSKY, R., BATAT, A. & BERCOVICI, B. **Antistrep lysin O Titer in Cord Blood.** *J. Immunolo* 1960, Jan., v. 84, No. 1, 54–7, 1 fig. [15 refs.]

"1. Fifty maternal and corresponding cord sera w examined for their ASLO content. A considera higher titer was found in 86% of the cord sera.

"2. The SLO inhibiting effect was totally neutralized in maternal as well as in cord sera by SLO.

"3. A nonspecific SLO inhibitor was not found in cord serum.

"4. Sera contaminated with *Pseudomonas aeruginosa* and sera undergoing alkaline hydrolysis developed very strong SLO inhibitory power. The factor concerned could not be absorbed by SLO.

"5. Total and free cholesterol levels were much higher in maternal than in cord sera."

MORRIS, B. **Transmission of Passive Immunity in an Insectivore.** [Correspondence.] *Nature.* 1959, Oct. 10, v. 184, Suppl. No. 15, 1151.

The method of transmission of immunity from the mother to the offspring in different animal species is discussed and it is claimed that transmission is either through the colostrum in suckling after birth or in some species by a peculiar relationship of the yolk sac to the uterus.

It was shown that the young of the hedgehog had no demonstrable anti-*Brucella* agglutinin in their sera before suckling notwithstanding a titre of 1:640 or more in the serum of the mother. *J. W. McLeod*

BURNET, M. **The Clonal Selection Theory of Acquired Immunity.**

This book is reviewed in this *Bulletin*, 1959, v. 34, 1310.

Book Reviews

BURN, J. L. [M.D., D.Hy., D.P.H.] **Recent Advances in Public Health.** 2nd Edition. pp. xi + 370, 54 figs. 1959. London: J. & A. Churchill Ltd. 104, Gloucester Place, W.1. [40s.]

The author of this volume in the *Recent Advances* series, a well-known figure in British public health, is Medical Officer of Health for the City of Salford, Lancashire (population: 178,000).

The present publication is the second edition of this book. The first edition was published 12 years ago [this *Bulletin*, 1947, v. 22, 674], a fact of some significance because, in 1947, the National Health Service in Britain had not come into being. In his Preface to the present edition, Dr. Burn tells us that "No attempt has been made to include, as in the former edition, accounts of advances made in water purification and in some other aspects of environmental sanitation". He goes on to say that more emphasis has been placed on the personal aspects of public health "and of those services which will help the individual in the pursuit of happiness and the 'good life'". He explains also that his book "does not aim to deal with the wide and deep issues of social medicine".

Few readers will quarrel with the author's own assessment of the book's objective, or with his statement that his endeavour has been "to provide the reader with an . . . account of some of the advances made in the practical day-to-day working of public health services at local level".

Many of the book's 370 pages are devoted to practical problems of co-operation within the National Health Service, and to an account of the duties and functions of various members of the public health team. In effect, the book is mainly an account of the way some parts of the National Health Service and allied services are working 10 years after their inception.

Chapter 13 is devoted to certain aspects of epidemiology, and Chapter 14 to some aspects of environmental hygiene. Though these chapters (like the rest of the book) are eminently readable, neither is, or purports to be, a substantial or complete chronicle of recent advances in the fields in question.

The reader will find in the chapters mentioned short accounts of immunization procedures, air pollution, food hygiene, radiation hazards, and other specific preventive and sanitary subjects, but it is not for the consideration of these subjects that the book can be recommended. Its main contribution will be to convey to the younger reader at home, and to interested readers of all ages abroad, something of the principles and aims of the National Health Service in Britain, and the spirit which motivates its operation in the homes of the people.

The book is beautifully produced, well illustrated, and handles well. It contains useful lists of references, important papers and recent books, which in some measure compensate for the admittedly thin treatment of important technical aspects of public health practice.

The second edition of *Recent Advances in Public Health* is not a text book. It is not a volume for the serious student who wants a balanced account of recent advances in public health practice in a single book. It is, however, a book which will be read with ease and pleasure for the purposes the author specifies in his Preface. *F. Grundy*

GILBERT, Jules. [B.A., M.D., D.P.H.] **Education sanitaire. Théorie et pratique.** [Health Education. Theory and Practice] With a preface by Armand FRAPPIER, O.B.E., B.A., M.D., L.Sc. 253 pp. 1959. Paris (VI^{e}): Masson et Cie., 120 Boulevard Saint-Germaine, France.

This book is a guide to the principles, practice and organization of health education. It is stated that all

public health workers should be health educators and should be trained to that end. The author emphasizes the inescapable part played by every doctor in health education, yet in many countries only those who have taken public health qualifications have had any training in this art. Health education is now recognized as being probably the most important agent in changing the habits favouring development of the chronic stress diseases which are the major medical problem in more advanced societies. This volume was written primarily for health educators working in the Province of Quebec, but the author expresses the hope that it will be useful to hygienists at all levels, and he has covered carefully all the methods employed.

Though health education is most effective when carried on through individual direct contact, this must be supplemented by instruction of groups and communities and even by mass education by radio or television. All educational methods must be used and co-ordinated to produce an effective propaganda organization. The most important function of all is to educate the teachers and this should be done during their training by a highly qualified full-time health educator. Health education in the schools forms an essential basis and one important result is that the adults of the future are much more susceptible to propaganda. While individual contact is the most effective form of health education and mass campaigns through press and radio are least effective, television, although it is similarly widely disseminated, is almost as effective as direct contact because of the audio-visual bond between the viewer and the televised speaker.

All aspects of health education are covered in 24 chapters. The first 15 are concerned with general principles, functions, organization, and selection and training of personnel. The outlook is very practical and the text is enriched by examples from the author's long experience in Quebec. The last 9 chapters deal with the various techniques of diffusing health education. The book is written mainly for countries in which the principal communicable diseases have been controlled, and it is pointed out that in such communities health education is more difficult because there is no specific remedy for the medical problems, and advances in control of disease depend almost entirely on change in people's way of living. There is, nevertheless, an excellent section on health education among illiterates.

Doctors rarely make good educators because they are interested primarily in medicine and not in establishing an emotional link with the pupil, which is essential in a good propagandist. Doctors and the various grades of health workers will find this book valuable for the thorough and very practical way in which all aspects of health education are covered. Each chapter ends with a useful list of references to books and journals in English or French. In an appendix the information to be collected on taking up a post is detailed, and a list of the questions which should be answered in assessing the results of a campaign. Professor Armand FRAPPIER of the School of Hygiene, University of Montreal, contributes a preface. *T. H. Davey*

MARTIN, J. H. [Editor.] **Radiation Biology. Proceedings of the Second Australasian Conference Radiation Biology held at the Universit Melbourne, 15–18 December, 1958, by t Australian Radiation Society.** pp. xi + 3(illustrated. 1959. New York 3: Academic Pr Inc., 111, Fifth Avenue, N.Y. London: Butt worths Scientific Publications, 4 & 5, Bell Ya W.C.2. [$11.00; 63s.]

This book contains 29 original articles, with a fo word by SIR F. MACFARLANE BURNET who poses questions for consideration by the symposium, all pe nent to the solution of the many problems present to those whose aim is to get to grips quantitativ with the action of ionizing radiation upon biologi processes.

The reader is quickly struck by the wide range material presented, some of which is not at once a preciated as being germane to the issue; for exam *Imperfections Induced in Solids by Fast-Particle Irrad tion* (pp. 272–281), but such a contribution will doubtl fit on to the foundation work upon the biologi problems.

The jacket of the book is illustrated by a mic photograph of the mouse duodenum; this, reproduc on p. 222, is the only one of its kind in the boo Cytologists will look in vain for articles upon visi cellular changes induced by radiation. This book is n about these things, but largely about the proces which bring well known changes about. It is in ma respects very mechanistic, and this represents t modern experimental approach, *viz.* every qualitat finding should be explored quantitatively.

The main subject matter can be grouped broadly convenience here, as follows: Leukaemia (2 article Bone marrow (2), Homografts (2), Role of Oxygen (Synthesis of Simple Organic Compounds (3), Stronti Deposition, Radioactive Fall-out and Fission Produ (2), Recovery from Radiation (3), Mutagens (2), a for those who wish to keep up with present tren of thought, there is a final article entitled *Radiob logical Mechanisms at the Cellular Level* (pp. 282–2

It is safe to say that all radiologists will find so articles to interest them, and not the least interesti portions of the book are those containing the discussio which followed the papers. One can sense h stimulating these must have been to all who pa cipated and in many cases very profitable to the per whose paper invoked them. *S. Rus.*

BURNET, F. M. & STANLEY, W. M. [Edited by.] **T Viruses. Biochemical, Biological and Biophy cal Properties. Vol. 3. Animal Virus** pp. xvii + 428, illustrated. 1959. New York Academic Press Inc., 111, Fifth Avenue, N London: 40, Pall Mall, S.W.1. [$12.00; 86s.]

The present work is the last of a series of 3 volu devoted to a presentation of general topics in virolo and is concerned with the animal viruses. There 13 sections, each of which is arranged as an individ

nonograph. In an introductory chapter the classification of the animal viruses is briefly presented by F. M. Burnet (pp. 1–14); the psittacosis group is included, nd it is pointed out that the morphological complexity f vaccinia virus makes it difficult to deny that it is micro-organism. Haemagglutination is dealt with in comprehensive chapter by S. G. ANDERSON (pp. 21–0), who divides the haemagglutinating viruses into 3 roups, according to whether the virus particle both gglutinates and elutes (myxoviruses), agglutinates without eluting (arborviruses), or is associated with an ndependent agglutinin (pox viruses). The present state f knowledge of virus receptors is almost entirely based n the observations of A. GOTTSCHALK, who describes is work on *N*-acetylneuraminic acid and the mucoroteins which are concerned in haemagglutination by nfluenza virus (pp. 51–61).

The aspect of virology which is probably advancing most rapidly at the present time is the study of the morphology of virus particles in the electron microscope, which is next described in a chapter by F. B. BANG (pp. 63–110). The inhibition of virus multiplication is described by F. L. HORSFALL Jr. (pp. 195–224); perusal of this chapter only serves to accentuate the act that antiviral chemotherapy has not yet reached he practical stage, since none of the many compounds mentioned have an antiviral activity of the order equired for clinical application. Other subjects dealt with include interference, variation and virus genetics, nd the book ends with an account of the insect viruses y K. M. SMITH (pp. 369–392).

The work is clearly designed for the research virologist, who will find it a necessary source book.

D. J. Bauer

BURNET, F. M. & STANLEY, W. M. [Edited by.] **The Viruses. Biochemical, Biological and Biophysical Properties. Vol. 2. Plant and Bacterial Viruses.** pp. xvi + 408, illustrated. 1959. New York 3: Academic Press Inc., 111, Fifth Avenue, N.Y. London: 40 Pall Mall, S.W.1. [93s.]

This book on viruses is not a textbook so much as a group of reviews from various contributors. It resembles in fact a volume of the series *Advances in Virus Research* from the same publishers, though the subjects reviewed are wider and the contributors to this book on the whole assume that the reader has no specialist knowledge. The first four chapters deal with plant viruses. In one, S. G. WILDMAN gives a general account which would be useful to anyone working on animal viruses who sometimes regrets his ignorance of the related subject. The chapter by R. MARKHAM on the biochemistry of plant viruses also contains a useful and clearly written section on nucleic acids, their structure and properties and their function in viruses. It was of course with tobacco mosaic virus that nucleic acid extracted from a virus was first shown to be infective, and a critical account of this work is given. The other two chapters on plant viruses deal with variation and its chemical correlates (C. A. KNIGHT) and biological cycles in insects (L. M. BLACK).

The section on bacteriophages is introduced by A. LWOFF with an essay on phage as a model of the host virus relationship. He develops a stimulating argument about the origin of bacteriophages, their inclusion in the virus group, the significance of infectivity and pathogenicity in the definition of a virus, coming to the inescapable conclusion that a virus can only be defined as a virus.

The remaining chapters are more factual. The initiation of phage infection is fully described by A. GAREN and L. M. KOZLOFF. They discuss the attachment of the phage to the host cell, the factors affecting it, and the mechanism of invasion up to the release of phage DNA. The next stages in intracellular multiplication are considered by G. S. STENT, from the eclipse phase through the synthesis of phage precursor substances and the fate of the infecting particles to the maturation of the new particles. This description is inevitably confined to virulent phages (the T phages) but the phenomenon of lysogeny receives a chapter to itself, contributed by F. JACOB and E. L. WOLLMAN. They cover the detection and occurrence of lysogeny as well as the properties of the temperate phage and the lysogenic bacterium. The chapter ends with an account of the authors' own work on the location of the prophage on the bacterial chromosome. For readers unfamiliar with the genetics of any group, C. LEVINTHAL contributes a general chapter on the genetics of bacteriophages. He describes the kinds of mutation known, the techniques of crossing, the nature and advantages of Benzer's r II system which has produced such important results, and how to make a linkage map. Finally, F. W. STAHL writes about phage radiobiology, including work done with U-V light, ionizing radiations and the incorporation of radioactive phosphorus into phage DNA. He also discusses work done on the recovery of phage genetic material damaged by these agents, by such methods as multiplicity and cross-reactivation, and by photoreactivation.

This volume covers the ground briefly indicated here in great detail. It is well documented and provides a useful reference book to some aspects of bacteriophage biology.

Janice Taverne

DALRYMPLE-CHAMPNEYS, Weldon [C.B., D.M., D.P.H., F.R.C.P.] *Brucella* **Infection and Undulant Fever in Man.** pp. xii + 196, frontispiece & 20 figs. 1960. New York. Toronto. London: Oxford University Press, Amen House, Warwick Square, E.C.4. [25s.]

The author has been a serious student of brucellosis for very many years; he is very familiar with the world literature on all aspects of the subject, but his particular interest has been the human disease—undulant fever—as seen in Britain. Over a period of more than 30 years he has collected the records of a great many cases and from these, excluding infections contracted abroad or in the laboratory, he has used the first 1,500 cases as the clinical basis in connexion with the production of this book. As he says in his preface, his object has been to provide a book of moderate size and cost, giving an account of brucella infection in man, its origin, the nature of the infecting organism, the clinical features of the disease it may produce, its

pathology, prevention, diagnosis, prognosis and treatment. There can be little doubt that the author has achieved his object; he has written a concise little manual on brucellosis, eminently readable, accurate on all the important issues, which has been well-produced in a convenient form. It contains an immense amount of information in less than 160 pages of text, well documented and with a subject and author index. Nevertheless it cannot be regarded as a reference book covering the whole field of brucellosis; it is primarily concerned with the clinical condition of undulant fever, its diagnosis and treatment, which is very fully considered. But it is by no means an ill-balanced book; the comparative pathology and bacteriology are, for instance, dealt with reasonably well. Indeed it is surprising to find so much detailed consideration given to serological diagnostic methods. This the reviewer thinks unfortunate, for it has led the author to rather dangerous ground when he implies, for example, that the Brucella Agglutinable Suspensions used by the Public Health Laboratory Service, although possessing approximately the same degree of agglutinability over the years, were not properly standardized. The reason for the constancy is that the Standards Laboratory for Serological Reagents, who prepare these suspensions, standardized every batch issued against a standard *Brucella abortus* serum made many years before the introduction of the International Standard Serum. But this is a very small point.

Sir Weldon is in his own field when he conside the clinical features of undulant fever where the weal of his own experience, supported by his very extensi knowledge of the literature, gives these chapters special value and interest.

There are nearly 400 references which are identifie in the text by numbers in brackets, often without tl author's name. The constant turning of the pages find the author's name and the date of the referen can be a little tiresome and one wishes the more usu system had been adopted. The author index can used with advantage in finding text references, but tl subject index is not so valuable.

The fact that Sir Weldon's collection of 1,500 inc genous cases was used as the clinical basis in preparir this book must not be taken to imply that undula fever as seen in other countries receives scant attentio The author treats brucella infections as a wor problem and is constantly referring to observations pu lished by foreign workers. But it is obvious in a boo of this size and design that such references are intr duced to illustrate a particular point, and in gener this has been done adequately.

The author is to be congratulated on the result his endeavours and the book can be read with intere from cover to cover, and it would probably be greater value to the reader who does this than to o who treats it as a reference book and dips into here and there. He may miss something of importanc

H. J. Bensted

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